GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 4, 2004, 15:21:50 ; Search time 1.61702 Seconds
(without alignments)
1397.867 Million cell updates/sec

Title: US-09-668-314C-84
Perfect score: 41
Sequence: 1 LVFFAEDF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1586107 seqs, 282547505 residues

Total number of hits satisfying chosen parameters: 1586107

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : A_Geneseq_29Jan04:*
1: geneseqp1980s:*
2: geneseqp1990s:*
3: geneseqp2000s:*
4: geneseqp2001s:*
5: geneseqp2002s:*
6: geneseqp2003as:*
7: geneseqp2003bs:*
8: geneseqp2004s:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	41	100.0	8	4	AAE10662	Aae10662 Human amy
2	41	100.0	8	4	AAE02614	Aae02614 Human amy
3	35	85.4	8	2	AAR08190	Aar08190 Cerebrova
4	35	85.4	8	2	AAW32551	Aaw32551 Amyloidog
5	35	85.4	8	4	AAE10663	Aae10663 Human amy
6	35	85.4	8	4	AAE02615	Aae02615 Human amy
7	35	85.4	8	5	ABB78624	Abb78624 Human alp
8	35	85.4	8	5	ABB78623	Abb78623 Human alp
9	35	85.4	8	6	ABU09765	Abu09765 Amyloidog

10	35	85.4	8	6	ABR61959	Abr61959 Human amy
11	35	85.4	8	7	ABW00134	Abw00134 Beta-amyl
12	35	85.4	9	6	ABU79063	Abu79063 Aggregati
13	35	85.4	9	7	ABW00197	Abw00197 Peptide #
14	35	85.4	10	3	AAY79938	Aay79938 Beta-amyl
15	35	85.4	10	4	AAB46229	Aab46229 Human APP
16	35	85.4	10	4	AAB46226	Aab46226 Human APP
17	35	85.4	10	4	AAB46228	Aab46228 Human APP
18	35	85.4	10	4	AAB46227	Aab46227 Human APP
19	35	85.4	11	2	AAW32560	Aaw32560 Anti-amyl
20	35	85.4	11	4	AAM52586	Aam52586 Peptide #
21	35	85.4	11	5	AAU99431	Aau99431 Human amy
22	35	85.4	11	5	AAE29504	Aae29504 Amyloid b
23	35	85.4	11	6	ABU79013	Abu79013 Amyloidog
24	35	85.4	11	7	ABW00147	Abw00147 Amyloid-b
25	35	85.4	12	2	AAR60372	Aar60372 Beta-amyl
26	35	85.4	12	3	AAB10957	Aab10957 Bovine AD
27	35	85.4	12	6	AAE35466	Aae35466 Abeta pep
28	35	85.4	13	6	AAE35465	Aae35465 Abeta pep
29	35	85.4	13	6	AAE35467	Aae35467 Abeta pep
30	35	85.4	13	6	ADA37467	Ada37467 Human amy
31	35	85.4	14	4	AAE03423	Aae03423 Peptide c
32	35	85.4	14	6	ADA89887	Ada89887 Beta-A4 s
33	35	85.4	15	2	AAW02334	Aaw02334 Beta-amyl
34	35	85.4	15	2	AAW89358	Aaw89358 Beta-amyl
35	35	85.4	15	2	AAW89354	Aaw89354 Beta-amyl
36	35	85.4	15	5	ABG71014	Abg71014 Long form
37	35	85.4	15	5	ABB05162	Abb05162 Beta amyl
38	35	85.4	15	5	AAE26271	Aae26271 Human bet
39	35	85.4	15	6	ABU79057	Abu79057 Aggregati
40	35	85.4	15	6	ABU79064	Abu79064 Aggregati
41	35	85.4	15	6	ABU79058	Abu79058 Aggregati
42	35	85.4	15	6	ABU79055	Abu79055 Aggregati
43	35	85.4	15	6	ABU79056	Abu79056 Aggregati
44	35	85.4	15	6	ABU79062	Abu79062 Aggregati
45	35	85.4	15	7	ABW00192	Abw00192 Peptide #

ALIGNMENTS

RESULT 1
AAE10662
ID AAE10662 standard; peptide; 8 AA.
XX
AC AAE10662;
XX
DT 10-DEC-2001 (first entry)
XX
DE Human amyloid precursor protein substrate alpha-secretase peptide #1.
XX
KW Human; aspartyl protease 1; Asp1; amyloid precursor protein; APP;
KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;
KW alpha-secretase.
XX
OS Homo sapiens.

XX
FH Key Location/Qualifiers
FT Cleavage-site 4. .5
FT Misc-difference 8
FT /note= "This residue is given as Val in the sequence
FT shown as SEQ ID NO: 72 in pages 92 and 160 of the
FT specification"
XX
PN GB2357767-A.
XX
PD 04-JUL-2001.
XX
PF 22-SEP-2000; 2000GB-00023315.
XX
PR 23-SEP-1999; 99US-00404133.
PR 23-SEP-1999; 99US-0155493P.
PR 23-SEP-1999; 99WO-US020881.
PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowkski MJ, Gurney M;
XX
DR WPI; 2001-444208/48.
XX
PT Polypeptide comprising fragments of human aspartyl protease with amyloid
PT precursor protein processing activity and alpha-secretase activity, for
PT identifying modulators useful in treating Alzheimer's disease.
XX
PS Claim 10; Page 163; 187pp; English.
XX
CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1
CC proteins which lack transmembrane domain or amino terminal domain or
CC cytoplasmic domain and retains alpha-secretase activity and amyloid
CC protein precursor (APP) processing activity. The proteins of the
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity
CC are useful for treating Alzheimer's disease (AD) which causes progressive
CC dementia with consequent formation of amyloid plaques, neurofibrillary
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein
CC with the substrate under acidic conditions and determining the level of
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid
CC precursor protein (APP) substrate alpha-secretase peptide which is used
CC for determining the enzymatic activity of Asp-1 protein lacking
CC transmembrane domain (TM) and containing a (His)6 tag. Note: The present
CC sequence shown in page 163 of the specification is stated as being the
CC same as that shown in page 92 and page 160 of the specification. However
CC the sequence differs at the C-terminal end
XX
SQ Sequence 8 AA;

Query Match 100.0%; Score 41; DB 4; Length 8;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 8; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAEDF 8
              ||||||||
Db          1 LVFFAEDF 8


RESULT 2
AAE02614
ID   AAE02614 standard; peptide; 8 AA.
XX
AC   AAE02614;
XX
DT   10-AUG-2001  (first entry)
XX
DE   Human amyloid precursor protein substrate alpha-secretase peptide #1.
XX
KW   Human; alpha-secretase; amyloid precursor protein; APP; therapy;
KW   Alzheimer's disease; antialzheimer's; aspartyl protease 1; Asp1;
KW   beta-secretase.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Cleavage-site   4. .5
XX
PN   WO200123533-A2.
XX
PD   05-APR-2001.
XX
PF   22-SEP-2000; 2000WO-US026080.
XX
PR   23-SEP-1999;   99US-0155493P.
PR   23-SEP-1999;   99WO-US020881.
PR   13-OCT-1999;   99US-00416901.
PR   06-DEC-1999;   99US-0169232P.
XX
PA   (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI   Gurney M,  Bienkowski MJ;
XX
DR   WPI; 2001-290516/30.
XX
PT   Enzymes that cleave the alpha-secretase site of the amyloid precursor
PT   protein, useful for the treatment of Alzheimer's disease.
XX
PS   Claim 10; Page 98; 189pp; English.
XX
CC   The present invention relates to enzymes for cleaving the alpha-
CC   secretase site of the amyloid precursor protein (APP) and methods of
CC   identifying those enzymes. The methods may be used to identify enzymes
CC   that may be used to cleave the alpha-secretase cleavage site of the APP
CC   protein. The enzymes may be used to treat or modulate the progress of
CC   Alzheimer's disease. The present sequence is human amyloid precursor
CC   protein (APP) substrate alpha-secretase peptide which is used for
CC   determining the enzymatic activity of Asp-1 deltaTM (His)6 protein. Note:
CC   The present sequence shown in page 98 of the specification is stated as
CC   being the same as that shown in page 94 and page 188 of the
```

CC specification. However the sequence differs at the C-terminal end
XX
SQ Sequence 8 AA;

  Query Match   100.0%; Score 41; DB 4; Length 8;
  Best Local Similarity   100.0%; Pred. No. 1.4e+06;
  Matches   8; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 LVFFAEDF 8
              ||||||||
Db   1 LVFFAEDF 8

RESULT 3
AAR08190
ID AAR08190 standard; peptide; 8 AA.
XX
AC AAR08190;
XX
DT 25-MAR-2003 (revised)
DT 09-JAN-2003 (revised)
DT 13-FEB-1991 (first entry)
XX
DE Cerebrovascular amyloid peptide.
XX
KW Down's Syndrome; Alzheimer's; monoclonal antibody; amyloid plaques;
KW beta-amyloid precursor.
XX
OS Synthetic.
XX
PN WO9012870-A.
XX
PD 01-NOV-1990.
XX
PF 14-APR-1989; 89US-00338302.
XX
PR 14-APR-1989; 89US-00338302.
XX
PA (REME-) RES FOUND MENTAL HYGIENE INC.
XX
PI Kim KS, Wisniewski HM, Miller DL, Sapienza VJ, Eqbal IG;
PI Chen CMJ;
XX
DR WPI; 1990-348473/46.
XX
PT New monoclonal antibodies to peptide(s) associated with downs syndrome -
PT esp. to cerebrovascular amyloid protein, useful for diagnosis of the
PT diseases in body fluids.
XX
PS Claim 9; Page 17; 25pp; English.
XX
CC This synthetic peptide is elevated in individuals with Down's Syndrome
CC (DS) or Alzheimer's disease (AD). Monoclonal antibodies raised against it
CC are useful for the non-invasive diagnosis of DS and AD and in the study
CC of the beta-amyloid precursor protein. (Updated on 09-JAN-2003 to add
CC missing OS field.) (Updated on 25-MAR-2003 to correct PA field.)
XX

```
SQ   Sequence 8 AA;

  Query Match             85.4%;  Score 35;  DB 2;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 1.4e+06;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          1 LVFFAED 7


RESULT 4
AAW32551
ID   AAW32551 standard; peptide; 8 AA.
XX
AC   AAW32551;
XX
DT   21-JAN-1998  (first entry)
XX
DE   Amyloidogenic sequence amyloid beta-peptide.
XX
KW   Anti-amyloid peptide; iAbeta; abnormal protein folding inhibitor;
KW   Alzheimer's disease; dementia; Down's syndrome; amyloidosis disorder;
KW   human prion disease; Kuru; Creutzfeldt-Jakob disease;
KW   Gerstmann-Straussler-Scheinker Syndrome; animal prion disease;
KW   prion associated human neurodegenerative disease; scrapie;
KW   spongiform encephalopathy; transmissible mink encephalopathy;
KW   chronic wasting disease; mule; deer; elk; human.
XX
OS   Homo sapiens.
OS   Synthetic.
XX
PN   WO9639834-A1.
XX
PD   19-DEC-1996.
XX
PF   06-JUN-1996;   96WO-US010220.
XX
PR   07-JUN-1995;   95US-00478326.
PR   10-APR-1996;   96US-00630645.
XX
PA   (UYNY ) UNIV NEW YORK STATE.
XX
PI   Soto-Jara C,  Baumann MH,  Frangione B;
XX
DR   WPI; 1997-051637/05.
XX
PT   New inhibitors of fibrillogenesis proteins or peptides - used for
PT   preventing, treating or detecting amyloidosis disorders such as
PT   Alzheimer's disease.
XX
PS   Disclosure; Fig 1A; 63pp; English.
XX
CC   A method has been developed for the prevention or treatment of a disorder
CC   or disease associated with the formation of amyloid or amyloid-like
CC   deposits, involving the abnormal folding of a protein or peptide. The
CC   method involves administering an inhibitory peptide which prevents the
```

CC abnormal folding or which dissolves existing amyloid or amyloid-like
CC deposits, where the peptide comprises a sequence of 3-15 amino acid
CC residues and has a hydrophobic cluster of at least 3 amino acids, where
CC at least one of the 3 amino acids is a beta-sheet blocking amino acid
CC residue selected from Pro, Gly, Asn and His. The present sequence
CC represents an amyloidogenic sequence, amyloid beta- peptide, which is
CC involved in the formation of several amyloid deposits. The inhibitory
CC peptide is capable of associating with a structural determinant on the
CC protein or peptide to structurally block and inhibit the abnormal folding
CC into amyloid or amyloid-like deposits. The method can be used for
CC preventing, treating or detecting e.g. Alzheimer's dementia or disease,
CC Down's syndrome, other amyloidosis disorders, human prion diseases such
CC as Kuru, Creutzfeldt-Jakob disease, Gerstmann- Straussler-Scheinker
CC Syndrome, prion associated human neurodegenerative diseases or animal
CC prion diseases such as scrapie, spongiform encephalopathy, transmissible
CC mink encephalopathy and chronic wasting disease of mule deer and elk
XX
SQ Sequence 8 AA;

Query Match 85.4%; Score 35; DB 2; Length 8;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
|||||||
Db 2 LVFFAED 8

RESULT 5
AAE10663
ID AAE10663 standard; peptide; 8 AA.
XX
AC AAE10663;
XX
DT 10-DEC-2001 (first entry)
XX
DE Human amyloid precursor protein substrate alpha-secretase peptide #2.
XX
KW Human; aspartyl protease 1; Asp1; amyloid precursor protein; APP;
KW Alzheimer's disease; AD; dementia; neurofibrillary tangle; gliosis;
KW amyloid plaque; neuronal loss; proteolytic; nootropic; neuroprotective;
KW alpha-secretase.
XX
OS Homo sapiens.
XX
FH Key Location/Qualifiers
FT Cleavage-site 4. .5
XX
PN GB2357767-A.
XX
PD 04-JUL-2001.
XX
PF 22-SEP-2000; 2000GB-00023315.
XX
PR 23-SEP-1999; 99US-00404133.
PR 23-SEP-1999; 99US-0155493P.
PR 23-SEP-1999; 99WO-US020881.

PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowkski MJ, Gurney M;
XX
DR WPI; 2001-444208/48.
XX
PT Polypeptide comprising fragments of human aspartyl protease with amyloid
PT precursor protein processing activity and alpha-secretase activity, for
PT identifying modulators useful in treating Alzheimer's disease.
XX
PS Claim 10; Page 163; 187pp; English.
XX
CC The patent discloses human aspartyl protease 1 (hu-Asp1) or modified Asp1
CC proteins which lack transmembrane domain or amino terminal domain or
CC cytoplasmic domain and retains alpha-secretase activity and amyloid
CC protein precursor (APP) processing activity. The proteins of the
CC invention are useful for assaying hu-Asp1 alpha-secretase activity, which
CC in turn is useful for identifying modulators of hu-Asp1 alpha-secretase
CC activity, where modulators that increase hu-Asp1 alpha-secretase activity
CC are useful for treating Alzheimer's disease (AD) which causes progressive
CC dementia with consequent formation of amyloid plaques, neurofibrillary
CC tangles, gliosis and neuronal loss. Hu-Asp1 protease substrate is useful
CC for assaying hu-Asp1 proteolytic activity, by contacting hu-Asp1 protein
CC with the substrate under acidic conditions and determining the level of
CC hu-Asp1 proteolytic activity. The present sequence is human amyloid
CC precursor protein (APP) substrate alpha-secretase peptide which is used
CC for determining the enzymatic activity of Asp-1 protein lacking
CC transmembrane domain (TM) and containing a (His)6 tag
XX
SQ Sequence 8 AA;

  Query Match   85.4%; Score 35; DB 4; Length 8;
  Best Local Similarity   100.0%; Pred. No. 1.4e+06;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 LVFFAED 7
              |||||||
Db   2 LVFFAED 8

RESULT 6
AAE02615
ID AAE02615 standard; peptide; 8 AA.
XX
AC AAE02615;
XX
DT 10-AUG-2001 (first entry)
XX
DE Human amyloid precursor protein substrate alpha-secretase peptide #2.
XX
KW Human; alpha-secretase; amyloid precursor protein; APP; therapy;
KW Alzheimer's disease; antialzheimer's; aspartyl protease 1; Asp1;
KW beta-secretase.
XX

OS Homo sapiens.
XX
FH Key   Location/Qualifiers
FT Cleavage-site   4. .5
XX
PN WO200123533-A2.
XX
PD 05-APR-2001.
XX
PF 22-SEP-2000; 2000WO-US026080.
XX
PR 23-SEP-1999; 99US-0155493P.
PR 23-SEP-1999; 99WO-US020881.
PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Gurney M, Bienkowski MJ;
XX
DR WPI; 2001-290516/30.
XX
PT Enzymes that cleave the alpha-secretase site of the amyloid precursor
PT protein, useful for the treatment of Alzheimer's disease.
XX
PS Claim 10; Page 98; 189pp; English.
XX
CC The present invention relates to enzymes for cleaving the alpha-
CC secretase site of the amyloid precursor protein (APP) and methods of
CC identifying those enzymes. The methods may be used to identify enzymes
CC that may be used to cleave the alpha-secretase cleavage site of the APP
CC protein. The enzymes may be used to treat or modulate the progress of
CC Alzheimer's disease. The present sequence is human amyloid precursor
CC protein (APP) substrate alpha-secretase peptide which is used for
CC determining the enzymatic activity of Asp-1 deltaTM (His)6 protein
XX
SQ Sequence 8 AA;

  Query Match   85.4%; Score 35; DB 4; Length 8;
  Best Local Similarity   100.0%; Pred. No. 1.4e+06;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 LVFFAED 7
              |||||||
Db   2 LVFFAED 8

RESULT 7
ABB78624
ID ABB78624 standard; peptide; 8 AA.
XX
AC ABB78624;
XX
DT 16-JUL-2002 (first entry)
XX
DE Human alpha secretase (Abeta12-28) peptide SEQ ID NO:73.
XX

KW Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic.
XX
OS Homo sapiens.
XX
PN GB2367060-A.
XX
PD 27-MAR-2002.
XX
PF 29-OCT-2001; 2001GB-00025934.
XX
PR 23-SEP-1999; 99US-00404133.
PR 23-SEP-1999; 99US-0155493P.
PR 23-SEP-1999; 99WO-US020881.
PR 13-OCT-1999; 99US-00416901.
PR 06-DEC-1999; 99US-0169232P.
PR 22-SEP-2000; 2000GB-00023315.
XX
PA (PHAA) PHARMACIA & UPJOHN CO.
XX
PI Bienkowkski MJ, Gurney M;
XX
DR WPI; 2002-397167/43.
XX
PT Human aspartyl protease 1 substrates useful in assays to detect aspartyl
PT protease activity, e.g. for the diagnosis of Alzheimer's disease.
XX
PS Example 15; Page 92; 182pp; English.
XX
CC The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC substrate (I) which comprises a peptide of no more than 50 amino acids,
CC and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC nucleotide sequence that hybridises under stringent conditions to the non
CC -coding strand complementary to a defined 1804 nucleotide sequence (see
CC ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1
CC proteolytic activity and lacks nucleotides encoding a transmembrane
CC domain); (3) a purified polynucleotide (III') comprising a sequence that
CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect
CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents a human alpha secretase peptide, which is used in an
CC example from the present invention
XX
SQ Sequence 8 AA;

Query Match 85.4%; Score 35; DB 5; Length 8;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;

```
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 8
ABB78623
ID   ABB78623 standard; peptide; 8 AA.
XX
AC   ABB78623;
XX
DT   16-JUL-2002  (first entry)
XX
DE   Human alpha secretase (Abeta12-28) peptide SEQ ID NO:72.
XX
KW   Human; Asp-1; Asp-2; aspartyl protease; Alzheimer's disease; proteolytic.
XX
OS   Homo sapiens.
XX
PN   GB2367060-A.
XX
PD   27-MAR-2002.
XX
PF   29-OCT-2001; 2001GB-00025934.
XX
PR   23-SEP-1999;   99US-00404133.
PR   23-SEP-1999;   99US-0155493P.
PR   23-SEP-1999;   99WO-US020881.
PR   13-OCT-1999;   99US-00416901.
PR   06-DEC-1999;   99US-0169232P.
PR   22-SEP-2000; 2000GB-00023315.
XX
PA   (PHAA ) PHARMACIA & UPJOHN CO.
XX
PI   Bienkowkski MJ,  Gurney M;
XX
DR   WPI; 2002-397167/43.
XX
PT   Human aspartyl protease 1 substrates useful in assays to detect aspartyl
PT   protease activity, e.g. for the diagnosis of Alzheimer's disease.
XX
PS   Example 15; Page 92; 182pp; English.
XX
CC   The present invention describes a human aspartyl protease 1 (hu-Asp1)
CC   substrate (I) which comprises a peptide of no more than 50 amino acids,
CC   and which comprises the 8 amino acid sequence Gly-Leu-Ala-Leu-Ala-Leu-
CC   Glu-Pro. Also described are: (1) a method (II) for assaying hu-Asp1
CC   proteolytic activity, comprising: (a) contacting a hu-Asp1 protein with
CC   (I) under acidic conditions; and (b) determining the level of hu-Asp1
CC   proteolytic activity; (2) a purified polynucleotide (III) comprising a
CC   nucleotide sequence that hybridises under stringent conditions to the non
CC   -coding strand complementary to a defined 1804 nucleotide sequence (see
CC   ABL52456) where the nucleotide sequence encodes a polypeptide having Asp1
CC   proteolytic activity and lacks nucleotides encoding a transmembrane
CC   domain); (3) a purified polynucleotide (III') comprising a sequence that
```

CC hybridises under stringent conditions to (III) (the nucleotide sequence
CC encodes a polypeptide further lacking a pro-peptide domain corresponding
CC to amino acids 23-62 of hu-Asp1 (see ABB78589)); (4) a vector (IV)
CC comprising (III) or (III'); and (5) a host cell (V) transformed or
CC transfected with (III), (III') and/or (IV). The hu-Asp1 protease
CC substrate (I) may be used as an enzyme substrate in assays to detect
CC aspartyl protease activity, (II) and therefore diagnose diseases
CC associated with aberrant hu-Asp1 expression and activity such as
CC Alzheimer's disease. Hu-Asp1 has been localised to chromosome 21, while
CC hu-Asp2 has been localised to chromosome 11q23.3-24.1. The present
CC sequence represents a human alpha secretase peptide, which is used in an
CC example from the present invention
XX
SQ Sequence 8 AA;

Query Match 85.4%; Score 35; DB 5; Length 8;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
|||||||
Db 1 LVFFAED 7

RESULT 9
ABU09765
ID ABU09765 standard; peptide; 8 AA.
XX
AC ABU09765;
XX
DT 17-JUN-2003 (first entry)
XX
DE Amyloidogenic Amyloid beta-peptide #1.
XX
KW Amyloid formation; amyloid-like deposit; Alzheimer's disease;
KW pathological beta-sheet-rich conformation; Down's syndrome;
KW amyloidosis disorder; human prion disease; kuru; CJD;
KW Creutzfeldt-Jakob disease; Gerstmann-Straussler-Scheinker syndrome; GSS;
KW prion associated human neurodegenerative disease; animal prion disease;
KW scrapie; spongiform encephalopathy; transmissible mink encephalopathy;
KW chronic wasting disease.
XX
OS Homo sapiens.
XX
PN US6462171-B1.
XX
PD 08-OCT-2002.
XX
PF 12-DEC-1996; 96US-00766596.
XX
PR 07-JUN-1995; 95US-00478326.
PR 10-APR-1996; 96US-00630645.
XX
PA (UYNY) UNIV NEW YORK STATE.
XX
PI Soto-Jara C, Baumann MH, Frangione B;
XX

DR WPI; 2003-379012/36.
XX
PT Novel inhibitory peptides which inhibit and structurally block abnormal
PT folding of protein into amyloid or amyloid-like deposit and into
PT pathological beta-sheet rich conformation, useful for treating
PT Alzheimer's disease.
XX
PS Example 1; Fig 1A; 51pp; English.
XX
CC The invention describes an isolated inhibitory peptide (I) which
CC interacts with a hydrophobic beta-sheet forming cluster of amino acid
CC residues on a protein or peptide for amyloid or amyloid-like deposit
CC formation, and inhibits or structurally blocks the abnormal folding of
CC proteins and peptides into amyloid or amyloid-like deposits and into
CC pathological beta-sheet-rich conformation. (I) is useful for disorders or
CC diseases associated with abnormal protein folding into amyloid or amyloid
CC -like deposits or into pathological beta-sheet-rich precursors of such
CC deposits, such as Alzheimer's disease, Down's syndrome, other amyloidosis
CC disorders, human prion diseases, such as kuru, Creutzfeldt-Jakob disease
CC (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS), prion associated
CC human neurodegenerative diseases as well as animal prion diseases such as
CC scrapie, spongiform encephalopathy, transmissible mink encephalopathy and
CC chronic wasting disease of mule deer and elk. (I) is also useful for
CC detecting and diagnosing the presence or absence of amyloid or amyloid-
CC like deposits in vivo and its precursors. This is the amino acid sequence
CC of peptide associated with the inhibition of amyloid or amyloid like
CC deposits
XX
SQ Sequence 8 AA;

  Query Match   85.4%; Score 35; DB 6; Length 8;
  Best Local Similarity   100.0%; Pred. No. 1.4e+06;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 LVFFAED 7
              |||||||
Db   2 LVFFAED 8

RESULT 10
ABR61959
ID ABR61959 standard; protein; 8 AA.
XX
AC ABR61959;
XX
DT 12-SEP-2003 (first entry)
XX
DE Human amyloid precursor protein (APP) fragment.
XX
KW Memapsin 1; nootropic; neuroprotective; memapsin 2; beta secretase;
KW beta-amyloid protein; Alzheimer's disease; amyloid precursor protein;
KW APP; human.
XX
OS Homo sapiens.
XX
PN WO2003039454-A2.
XX

PD 15-MAY-2003.
XX
PF 23-OCT-2002; 2002WO-US034324.
XX
PR 23-OCT-2001; 2001US-0335952P.
PR 27-NOV-2001; 2001US-0333545P.
PR 14-JAN-2002; 2002US-0348464P.
PR 14-JAN-2002; 2002US-0348615P.
PR 20-JUN-2002; 2002US-0390804P.
PR 19-JUL-2002; 2002US-0397557P.
PR 19-JUL-2002; 2002US-0397619P.
XX
PA (OKLA-) OKLAHOMA MEDICAL RES FOUND.
PA (UNII) UNIV ILLINOIS FOUND.
XX
PI Ghosh AK, Tang J, Bilcer G, Chang W, Hong L, Koelsch G, Loy J;
PI Turner RT;
XX
DR WPI; 2003-541410/51.
XX
PT New peptide compounds are memapsin beta secretase inhibitors used for
PT treating Alzheimer's disease.
XX
PS Example 2; Page 156; 407pp; English.
XX
CC The invention relates to peptide compounds of specified formula. The
CC compounds exhibit memapsin 2-beta secretase inhibitory activity relative
CC to memapsin 1-beta secretase and reduce the accumulation of beta-amyloid
CC protein. The compounds can be used for treating Alzheimer's disease. The
CC present sequence represents a human amyloid precursor protein (APP)
CC fragment where hydolysis by memapsin takes place
XX
SQ Sequence 8 AA;

Query Match 85.4%; Score 35; DB 6; Length 8;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
|||||||
Db 2 LVFFAED 8

RESULT 11
ABW00134
ID ABW00134 standard; peptide; 8 AA.
XX
AC ABW00134;
XX
DT 15-JAN-2004 (first entry)
XX
DE Beta-amyloid peptide.
XX
KW Amyloid-like fibril deposit; prion related encephalopathy; gene therapy;
KW Alzheimer's disease; beta-amyloid.
XX
OS Unidentified.

XX
PN US2003087407-A1.
XX
PD 08-MAY-2003.
XX
PF 06-SEP-2002; 2002US-00235483.
XX
PR 07-JUN-1995; 95US-00478326.
PR 10-APR-1996; 96US-00630645.
PR 12-DEC-1996; 96US-00766596.
XX
PA (UYNY) UNIV NEW YORK STATE.
XX
PI Soto-Jara C, Baumann MH, Frangione B;
XX
DR WPI; 2003-616149/58.
XX
PT New inhibitory peptide, useful for preparing a composition for
PT diagnosing, preventing or treating disorders associated with amyloid-like
PT fibril deposits, e.g. Alzheimer's disease, or prion related
PT encephalopathies.
XX
PS Example 1; Fig 1A; 52pp; English.
XX
CC The invention relates to inhibitory peptide comprising a portion of at
CC least three amino acid residues and a sequence predicted not to adopt a
CC beta-sheet structure that associates with a hydrophobic beta-sheet
CC cluster on a protein or peptide involved in the abnormal folding into a
CC beta-sheet structure, to structurally block the abnormal folding of the
CC protein or peptide. The inhibitory peptide is useful for preparing a
CC composition for preventing, treating or detecting disorders or diseases
CC associated with amyloid-like fibril deposits e.g. Alzheimer's disease and
CC prion related encephalopathies. The invention is also useful in gene
CC therapy. The present sequence is beta-amyloid peptide. This peptide is
CC involved in the formation of several amyloid deposits
XX
SQ Sequence 8 AA;

  Query Match   85.4%; Score 35; DB 7; Length 8;
  Best Local Similarity   100.0%; Pred. No. 1.4e+06;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 LVFFAED 7
              |||||||
Db   2 LVFFAED 8

RESULT 12
ABU79063
ID ABU79063 standard; peptide; 9 AA.
XX
AC ABU79063;
XX
DT 17-JUN-2003 (first entry)
XX
DE Aggregation blocking peptide #15.
XX

KW Amyloid formation; amyloid-like deposit; Alzheimer's disease;
KW pathological beta-sheet-rich conformation; Down's syndrome;
KW amyloidosis disorder; human prion disease; kuru; CJD;
KW Creutzfeldt-Jakob disease; Gerstmann-Straussler-Scheinker syndrome; GSS;
KW prion associated human neurodegenerative disease; animal prion disease;
KW scrapie; spongiform encephalopathy; transmissible mink encephalopathy;
KW chronic wasting disease.
XX
OS Unidentified.
XX
PN US6462171-B1.
XX
PD 08-OCT-2002.
XX
PF 12-DEC-1996; 96US-00766596.
XX
PR 07-JUN-1995; 95US-00478326.
PR 10-APR-1996; 96US-00630645.
XX
PA (UYNY) UNIV NEW YORK STATE.
XX
PI Soto-Jara C, Baumann MH, Frangione B;
XX
DR WPI; 2003-379012/36.
XX
PT Novel inhibitory peptides which inhibit and structurally block abnormal
PT folding of protein into amyloid or amyloid-like deposit and into
PT pathological beta-sheet rich conformation, useful for treating
PT Alzheimer's disease.
XX
PS Disclosure; Col 51-52; 51pp; English.
XX
CC The invention describes an isolated inhibitory peptide (I) which
CC interacts with a hydrophobic beta-sheet forming cluster of amino acid
CC residues on a protein or peptide for amyloid or amyloid-like deposit
CC formation, and inhibits or structurally blocks the abnormal folding of
CC proteins and peptides into amyloid or amyloid-like deposits and into
CC pathological beta-sheet-rich conformation. (I) is useful for disorders or
CC diseases associated with abnormal protein folding into amyloid or amyloid
CC -like deposits or into pathological beta-sheet-rich precursors of such
CC deposits, such as Alzheimer's disease, Down's syndrome, other amyloidosis
CC disorders, human prion diseases, such as kuru, Creutzfeldt-Jakob disease
CC (CJD), Gerstmann-Straussler-Scheinker syndrome (GSS), prion associated
CC human neurodegenerative diseases as well as animal prion diseases such as
CC scrapie, spongiform encephalopathy, transmissible mink encephalopathy and
CC chronic wasting disease of mule deer and elk. (I) is also useful for
CC detecting and diagnosing the presence or absence of amyloid or amyloid-
CC like deposits in vivo and its precursors. This is the amino acid sequence
CC of peptide associated with the inhibition of amyloid or amyloid like
CC deposits
XX
SQ Sequence 9 AA;

Query Match 85.4%; Score 35; DB 6; Length 9;
Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 13
ABW00197
ID   ABW00197 standard; peptide; 9 AA.
XX
AC   ABW00197;
XX
DT   15-JAN-2004  (first entry)
XX
DE   Peptide #15 used in the invention.
XX
KW   Amyloid-like fibril deposit; prion related encephalopathy; gene therapy;
KW   Alzheimer's disease.
XX
OS   Unidentified.
XX
PN   US2003087407-A1.
XX
PD   08-MAY-2003.
XX
PF   06-SEP-2002; 2002US-00235483.
XX
PR   07-JUN-1995;   95US-00478326.
PR   10-APR-1996;   96US-00630645.
PR   12-DEC-1996;   96US-00766596.
XX
PA   (UYNY ) UNIV NEW YORK STATE.
XX
PI   Soto-Jara C,  Baumann MH,  Frangione B;
XX
DR   WPI; 2003-616149/58.
XX
PT   New inhibitory peptide, useful for preparing a composition for
PT   diagnosing, preventing or treating disorders associated with amyloid-like
PT   fibril deposits, e.g. Alzheimer's disease, or prion related
PT   encephalopathies.
XX
PS   Claim 1; Page 28; 52pp; English.
XX
CC   The invention relates to inhibitory peptide comprising a portion of at
CC   least three amino acid residues and a sequence predicted not to adopt a
CC   beta-sheet structure that associates with a hydrophobic beta-sheet
CC   cluster on a protein or peptide involved in the abnormal folding into a
CC   beta-sheet structure, to structurally block the abnormal folding of the
CC   protein or peptide. The inhibitory peptide is useful for preparing a
CC   composition for preventing, treating or detecting disorders or diseases
CC   associated with amyloid-like fibril deposits e.g. Alzheimer's disease and
CC   prion related encephalopathies. The invention is also useful in gene
CC   therapy. The present sequence is a peptide used in the invention
XX
SQ   Sequence 9 AA;

  Query Match             85.4%;  Score 35;  DB 7;  Length 9;
```

Best Local Similarity 100.0%; Pred. No. 1.4e+06;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9
```

RESULT 14
AAY79938
ID AAY79938 standard; peptide; 10 AA.
XX
AC AAY79938;
XX
DT 11-MAY-2000 (first entry)
XX
DE Beta-amyloid recognition peptide SEQ ID NO:3.
XX
KW Beta-amyloid; inhibitor; recognition element; hybrid; aggregation;
KW Alzheimer's disease; neuroprotective; nootropic.
XX
OS Homo sapiens.
XX
PN US6022859-A.
XX
PD 08-FEB-2000.
XX
PF 14-NOV-1997; 97US-00970833.
XX
PR 15-NOV-1996; 96US-0030840P.
XX
PA (WISC) WISCONSIN ALUMNI RES FOUND.
XX
PI Murphy RM, Kiessling LL;
XX
DR WPI; 2000-160387/14.
XX
PT Beta-amyloid inhibitor useful for treating Alzheimer's disease.
XX
PS Example; Col 7; 15pp; English.
XX
CC The present invention describes a beta-amyloid inhibitor peptide. Beta-
CC amyloid inhibitors have neuroprotective and nootropic properties. The
CC inhibitor peptides are useful for the treatment of Alzheimer's disease.
CC The present sequence represents a beta-amyloid recognition peptide used
CC in the exemplification of present invention
XX
SQ Sequence 10 AA;

Query Match 85.4%; Score 35; DB 3; Length 10;
Best Local Similarity 100.0%; Pred. No. 1.4;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8
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RESULT 15
AAB46229
ID AAB46229 standard; peptide; 10 AA.
XX
AC AAB46229;
XX
DT 04-APR-2001 (first entry)
XX
DE Human APP derived immunogenic peptide #25.
XX
KW Amyloid deposit; APP; Abeta; brain; human; clearing response; nootropic;
KW Fc receptor mediated phagocytosis; immunogenic response; neuroprotective;
KW amyloid precursor protein; Alzheimer's disease.
XX
OS Homo sapiens.
XX
PN WO200072880-A2.
XX
PD 07-DEC-2000.
XX
PF 26-MAY-2000; 2000WO-US014810.
XX
PR 28-MAY-1999; 99US-00322289.
XX
PA (NEUR-) NEURALAB LTD.
XX
PI Schenk DB, Bard F, Vasquez NJ, Yednock T;
XX
DR WPI; 2001-032104/04.
XX
PT Preventing or treating a disease associated with amyloid deposits,
PT especially Alzheimer's disease, comprises administering amyloid specific
PT antibody.
XX
PS Disclosure; Fig 19; 143pp; English.
XX
CC This invention describes a novel method of preventing or treating a
CC disease associated with amyloid deposits of amyloid precursor protein
CC (APP) Abeta fragments in the brain of a patient, which comprises
CC administering to the patient: (a) an antibody that binds to Abeta, the
CC antibody binds to an amyloid deposit and induces a clearing response (Fc
CC receptor mediated phagocytosis) against it (b) a polypeptide containing
CC an N-terminal segment of at least residues 1-5 of Abeta; or (c) an agent
CC that induces an immunogenic response against residues 1-3 to 7-11 of
CC Abeta. The products of the invention have nootropic and neuroprotective
CC activity. The method is also useful for monitoring a course of treatment
CC being administered to a patient e.g. active and passive immunization. The
CC methods are useful for prophylactic and therapeutic treatment of
CC Alzheimer's disease
XX
SQ Sequence 10 AA;

  Query Match   85.4%; Score 35; DB 4; Length 10;
  Best Local Similarity   100.0%; Pred. No. 1.4;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 LVFFAED 7
              |||||||
Db          1 LVFFAED 7


Search completed: March  4, 2004, 15:35:45
Job time : 2.61702 secs
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GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 4, 2004, 15:31:20 ; Search time 0.519149 Seconds
(without alignments)
795.548 Million cell updates/sec

Title: US-09-668-314C-84
Perfect score: 41
Sequence: 1 LVFFAEDF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 389414 seqs, 51625971 residues

Total number of hits satisfying chosen parameters: 389414

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : Issued_Patents_AA:*
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2: /cgn2_6/ptodata/2/iaa/5B_COMB.pep:*
3: /cgn2_6/ptodata/2/iaa/6A_COMB.pep:*
4: /cgn2_6/ptodata/2/iaa/6B_COMB.pep:*
5: /cgn2_6/ptodata/2/iaa/PCTUS_COMB.pep:*
6: /cgn2_6/ptodata/2/iaa/backfiles1.pep:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	35	85.4	8	2	US-08-630-645-1	Sequence 1, Appli
2	35	85.4	8	4	US-08-766-596A-1	Sequence 1, Appli
3	35	85.4	8	5	PCT-US96-10220-1	Sequence 1, Appli
4	35	85.4	9	4	US-08-766-596A-64	Sequence 64, Appl
5	35	85.4	10	3	US-08-970-833-3	Sequence 3, Appli
6	35	85.4	11	2	US-08-630-645-14	Sequence 14, Appl
7	35	85.4	11	4	US-08-766-596A-14	Sequence 14, Appl
8	35	85.4	11	5	PCT-US96-10220-14	Sequence 14, Appl
9	35	85.4	12	1	US-08-302-808-11	Sequence 11, Appl
10	35	85.4	12	2	US-08-986-948-11	Sequence 11, Appl
11	35	85.4	14	4	US-09-458-481B-13	Sequence 13, Appl

12	35	85.4	14	4	US-09-594-366-5	Sequence 5, Appli
13	35	85.4	15	2	US-08-612-785B-14	Sequence 14, Appl
14	35	85.4	15	2	US-08-612-785B-37	Sequence 37, Appl
15	35	85.4	15	4	US-08-617-267C-14	Sequence 14, Appl
16	35	85.4	15	4	US-08-766-596A-56	Sequence 56, Appl
17	35	85.4	15	4	US-08-766-596A-57	Sequence 57, Appl
18	35	85.4	15	4	US-08-766-596A-58	Sequence 58, Appl
19	35	85.4	15	4	US-08-766-596A-59	Sequence 59, Appl
20	35	85.4	15	4	US-08-766-596A-63	Sequence 63, Appl
21	35	85.4	15	4	US-08-766-596A-65	Sequence 65, Appl
22	35	85.4	17	4	US-09-264-709A-2	Sequence 2, Appli
23	35	85.4	17	4	US-09-594-366-3	Sequence 3, Appli
24	35	85.4	19	3	US-08-970-833-11	Sequence 11, Appl
25	35	85.4	20	3	US-08-970-833-10	Sequence 10, Appl
26	35	85.4	26	1	US-08-304-585-7	Sequence 7, Appli
27	35	85.4	28	1	US-08-346-849-4	Sequence 4, Appli
28	35	85.4	28	1	US-08-302-808-7	Sequence 7, Appli
29	35	85.4	28	2	US-08-609-090-2	Sequence 2, Appli
30	35	85.4	28	2	US-08-986-948-7	Sequence 7, Appli
31	35	85.4	28	2	US-08-293-284A-4	Sequence 4, Appli
32	35	85.4	28	2	US-08-461-216-2	Sequence 2, Appli
33	35	85.4	28	3	US-09-388-890-2	Sequence 2, Appli
34	35	85.4	28	3	US-09-388-890-3	Sequence 3, Appli
35	35	85.4	28	3	US-09-388-890-4	Sequence 4, Appli
36	35	85.4	28	3	US-09-388-890-5	Sequence 5, Appli
37	35	85.4	28	3	US-09-388-890-6	Sequence 6, Appli
38	35	85.4	28	3	US-09-388-890-7	Sequence 7, Appli
39	35	85.4	28	3	US-09-388-890-8	Sequence 8, Appli
40	35	85.4	28	3	US-09-388-890-9	Sequence 9, Appli
41	35	85.4	28	3	US-09-388-890-10	Sequence 10, Appl
42	35	85.4	28	3	US-09-388-890-11	Sequence 11, Appl
43	35	85.4	28	3	US-09-388-890-14	Sequence 14, Appl
44	35	85.4	28	4	US-09-264-709A-1	Sequence 1, Appli
45	35	85.4	28	4	US-08-723-661B-2	Sequence 2, Appli

ALIGNMENTS

```
RESULT 1
US-08-630-645-1
; Sequence 1, Application US/08630645
; Patent No. 5948763
;  GENERAL INFORMATION:
;    APPLICANT:  SOTO-JARA, Claudio
;    APPLICANT:  BAUMANN, Marc
;    APPLICANT:  FRANGIONE, Blas
;    TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL COMPOSITIONS
;    TITLE OF INVENTION:  THEREOF FOR TREATMENT OF DISORDERS OR DISEASES
ASSOCIATED
;    TITLE OF INVENTION:  WITH PROTEIN FOLDING INTO AMYLOID OR AMYLOID-LIKE
DEPOSITS
;    NUMBER OF SEQUENCES:  26
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  BROWDY AND NEIMARK
;      STREET:  419 Seventh Street, N.W., Suite 400
;      CITY:  Washington
```

```
;       STATE:  D.C.
;       COUNTRY:  USA
;       ZIP:  20004
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.30
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/630,645
;       FILING DATE:
;       CLASSIFICATION:  530
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  US 08/478,326
;       FILING DATE:  06-JUN-1995
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  YUN, Allen C.
;       REGISTRATION NUMBER:  37,971
;       REFERENCE/DOCKET NUMBER:  SOTO-JARA=1
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  202-628-5197
;       TELEFAX:  202-737-3528
;   INFORMATION FOR SEQ ID NO:  1:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  8 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
US-08-630-645-1

  Query Match             85.4%;  Score 35;  DB 2;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 3e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 2
US-08-766-596A-1
; Sequence 1, Application US/08766596A
; Patent No. 6462171
;  GENERAL INFORMATION:
;     APPLICANT:  SOTO-JARA, Claudio
;     APPLICANT:  BAUMANN, Marc
;     APPLICANT:  FRANGIONE, Blas
;     TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL
;     TITLE OF INVENTION:  COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;     TITLE OF INVENTION:  ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;     TITLE OF INVENTION:  DEPOSITS
;     NUMBER OF SEQUENCES:  69
;     CORRESPONDENCE ADDRESS:
;       ADDRESSEE:  BROWDY AND NEIMARK
```

```
;       STREET:  419 Seventh Street, N.W., Suite 400
;       CITY:  Washington
;       STATE:  D.C.
;       COUNTRY:  USA
;       ZIP:  20004
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.30
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/766,596A
;       FILING DATE:
;       CLASSIFICATION:  435
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  US 08/630,645
;       FILING DATE:  10-APR-1996
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  US 08/478,326
;       FILING DATE:  06-JUN-1995
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  YUN, Allen C.
;       REGISTRATION NUMBER:  37,971
;       REFERENCE/DOCKET NUMBER:  SOTO-JARA=1A
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  202-628-5197
;       TELEFAX:  202-737-3528
;   INFORMATION FOR SEQ ID NO:  1:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  8 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
US-08-766-596A-1

  Query Match             85.4%;  Score 35;  DB 4;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 3e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 3
PCT-US96-10220-1
; Sequence 1, Application PC/TUS9610220
;  GENERAL INFORMATION:
;     APPLICANT:
;     TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL COMPOSITIONS
;     TITLE OF INVENTION:  THEREOF FOR TREATMENT OF DISORDERS OR DISEASES
ASSOCIATED
;     TITLE OF INVENTION:  WITH PROTEIN FOLDING INTO AMYLOID OR AMYLOID-LIKE
DEPOSITS
;     NUMBER OF SEQUENCES:  26
;     CORRESPONDENCE ADDRESS:
```

```
;       ADDRESSEE:  BROWDY AND NEIMARK
;       STREET:  419 Seventh Street, N.W., Suite 400
;       CITY:  Washington
;       STATE:  D.C.
;       COUNTRY:  USA
;       ZIP:  20004
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.30
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  PCT/US96/10220
;       FILING DATE:
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  US 08/478,326
;       FILING DATE:  06-JUN-1995
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  US 08/630,645
;       FILING DATE:  10-APR-1996
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  BROWDY, Roger L.
;       REGISTRATION NUMBER:  25,618
;       REFERENCE/DOCKET NUMBER:  SOTO-JARA=1 PCT
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  202-628-5197
;       TELEFAX:  202-737-3528
;   INFORMATION FOR SEQ ID NO:  1:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  8 amino acids
;       TYPE:  amino acid
;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
PCT-US96-10220-1

  Query Match             85.4%;  Score 35;  DB 5;  Length 8;
  Best Local Similarity   100.0%;  Pred. No. 3e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 4
US-08-766-596A-64
; Sequence 64, Application US/08766596A
; Patent No. 6462171
;  GENERAL INFORMATION:
;     APPLICANT:  SOTO-JARA, Claudio
;     APPLICANT:  BAUMANN, Marc
;     APPLICANT:  FRANGIONE, Blas
;     TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL
;     TITLE OF INVENTION:  COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
```

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;    TITLE OF INVENTION:  ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;    TITLE OF INVENTION:  DEPOSITS
;    NUMBER OF SEQUENCES:  69
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  BROWDY AND NEIMARK
;      STREET:  419 Seventh Street, N.W., Suite 400
;      CITY:  Washington
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20004
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/766,596A
;      FILING DATE:
;      CLASSIFICATION:  435
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/630,645
;      FILING DATE:  10-APR-1996
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/478,326
;      FILING DATE:  06-JUN-1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  YUN, Allen C.
;      REGISTRATION NUMBER:  37,971
;      REFERENCE/DOCKET NUMBER:  SOTO-JARA=1A
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-628-5197
;      TELEFAX:  202-737-3528
;  INFORMATION FOR SEQ ID NO:  64:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  9 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-766-596A-64

  Query Match             85.4%;  Score 35;  DB 4;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 3e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 5
US-08-970-833-3
; Sequence 3, Application US/08970833
; Patent No. 6022859
;  GENERAL INFORMATION:
;    APPLICANT:  Kiessling, Laura L.
```

```
;    APPLICANT:  Murphy, Regina M.
;    TITLE OF INVENTION:  INHIBITORS OF BETA-AMYLOID TOXICITY
;    NUMBER OF SEQUENCES:  11
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Quarles & Brady
;      STREET:  411 East Wisconsin Avenue
;      CITY:  Milwaukee
;      STATE:  Wisconsin
;      COUNTRY:  U.S.A.
;      ZIP:  53202-4497
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/970,833
;      FILING DATE:
;      CLASSIFICATION:  530
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Baker, Jean C.
;      REGISTRATION NUMBER:  35,433
;      REFERENCE/DOCKET NUMBER:  960296.94291
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (414) 277-5709
;      TELEFAX:  (414) 271-3552
;  INFORMATION FOR SEQ ID NO:  3:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  10 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-970-833-3

  Query Match             85.4%;  Score 35;  DB 3;  Length 10;
  Best Local Similarity   100.0%;  Pred. No. 0.42;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 6
US-08-630-645-14
; Sequence 14, Application US/08630645
; Patent No. 5948763
;  GENERAL INFORMATION:
;    APPLICANT:  SOTO-JARA, Claudio
;    APPLICANT:  BAUMANN, Marc
;    APPLICANT:  FRANGIONE, Blas
;    TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL COMPOSITIONS
;    TITLE OF INVENTION:  THEREOF FOR TREATMENT OF DISORDERS OR DISEASES
ASSOCIATED
;    TITLE OF INVENTION:  WITH PROTEIN FOLDING INTO AMYLOID OR AMYLOID-LIKE
DEPOSITS
```

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;    NUMBER OF SEQUENCES:  26
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  BROWDY AND NEIMARK
;      STREET:  419 Seventh Street, N.W., Suite 400
;      CITY:  Washington
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20004
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/630,645
;      FILING DATE:
;      CLASSIFICATION:  530
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/478,326
;      FILING DATE:  06-JUN-1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  YUN, Allen C.
;      REGISTRATION NUMBER:  37,971
;      REFERENCE/DOCKET NUMBER:  SOTO-JARA=1
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-628-5197
;      TELEFAX:  202-737-3528
;  INFORMATION FOR SEQ ID NO:  14:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  11 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-630-645-14

  Query Match             85.4%;  Score 35;  DB 2;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 0.46;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 7
US-08-766-596A-14
; Sequence 14, Application US/08766596A
; Patent No. 6462171
;  GENERAL INFORMATION:
;    APPLICANT:  SOTO-JARA, Claudio
;    APPLICANT:  BAUMANN, Marc
;    APPLICANT:  FRANGIONE, Blas
;    TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL
;    TITLE OF INVENTION:  COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
```

```
;    TITLE OF INVENTION:  ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;    TITLE OF INVENTION:  DEPOSITS
;    NUMBER OF SEQUENCES:  69
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  BROWDY AND NEIMARK
;      STREET:  419 Seventh Street, N.W., Suite 400
;      CITY:  Washington
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20004
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/766,596A
;      FILING DATE:
;      CLASSIFICATION:  435
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/630,645
;      FILING DATE:  10-APR-1996
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/478,326
;      FILING DATE:  06-JUN-1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  YUN, Allen C.
;      REGISTRATION NUMBER:  37,971
;      REFERENCE/DOCKET NUMBER:  SOTO-JARA=1A
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-628-5197
;      TELEFAX:  202-737-3528
;  INFORMATION FOR SEQ ID NO:  14:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  11 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
US-08-766-596A-14

  Query Match             85.4%;  Score 35;  DB 4;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 0.46;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 8
PCT-US96-10220-14
; Sequence 14, Application PC/TUS9610220
;  GENERAL INFORMATION:
;    APPLICANT:
;    TITLE OF INVENTION:  PEPTIDES AND PHARMACEUTICAL COMPOSITIONS
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```
;    TITLE OF INVENTION:  THEREOF FOR TREATMENT OF DISORDERS OR DISEASES
ASSOCIATED
;    TITLE OF INVENTION:  WITH PROTEIN FOLDING INTO AMYLOID OR AMYLOID-LIKE
DEPOSITS
;    NUMBER OF SEQUENCES:  26
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  BROWDY AND NEIMARK
;      STREET:  419 Seventh Street, N.W., Suite 400
;      CITY:  Washington
;      STATE:  D.C.
;      COUNTRY:  USA
;      ZIP:  20004
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  PCT/US96/10220
;      FILING DATE:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/478,326
;      FILING DATE:  06-JUN-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  US 08/630,645
;      FILING DATE:  10-APR-1996
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  BROWDY, Roger L.
;      REGISTRATION NUMBER:  25,618
;      REFERENCE/DOCKET NUMBER:  SOTO-JARA=1 PCT
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-628-5197
;      TELEFAX:  202-737-3528
;  INFORMATION FOR SEQ ID NO:  14:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  11 amino acids
;      TYPE:  amino acid
;      STRANDEDNESS:  single
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  peptide
PCT-US96-10220-14

  Query Match             85.4%;  Score 35;  DB 5;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 0.46;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 9
US-08-302-808-11
; Sequence 11, Application US/08302808
; Patent No. 5750349
;  GENERAL INFORMATION:
;    APPLICANT:  SUZUKI, No. 5750349uhiro
```

; APPLICANT: ODAKA, Asano
; APPLICANT: KITADA, Chieko
; TITLE OF INVENTION: ANTIBODIES TO B-AMYLOIDS OR THEIR
; TITLE OF INVENTION: DERIVATIVES AND USE THEREOF
; NUMBER OF SEQUENCES: 14
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: DIKE, BRONSTEIN, ROBERTS & CUSHMAN
; STREET: 130 WATER STREET
; CITY: BOSTON
; STATE: MA
; COUNTRY: USA
; ZIP: 02019
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Diskette
; COMPUTER: IBM Compatible
; OPERATING SYSTEM: DOS
; SOFTWARE: FastSEQ Version 1.5
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/08/302,808
; FILING DATE: 15-SEP-1994
; CLASSIFICATION: 435
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: PCT/JP94/00089
; FILING DATE: 24-JAN-1994
; APPLICATION NUMBER: 010132/1993
; FILING DATE: 25-JAN-1993
; APPLICATION NUMBER: 019035/1993
; FILING DATE: 05-FEB-1993
; APPLICATION NUMBER: 286985/1993
; FILING DATE: 16-NOV-1993
; APPLICATION NUMBER: 334773/1993
; FILING DATE: 28-DEC-1993
; ATTORNEY/AGENT INFORMATION:
; NAME: DAVID, RESNICK S
; REGISTRATION NUMBER: 34,235
; REFERENCE/DOCKET NUMBER: 44631
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 617-523-3400
; TELEFAX: 617-523-6440
; TELEX: 200291 STRE
; INFORMATION FOR SEQ ID NO: 11:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 12 amino acids
; TYPE: amino acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
; HYPOTHETICAL: NO
; ANTI-SENSE: NO
; FRAGMENT TYPE: N-terminal
; ORIGINAL SOURCE:
US-08-302-808-11

Query Match 85.4%; Score 35; DB 1; Length 12;
Best Local Similarity 100.0%; Pred. No. 0.51;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 LVFFAED 7
              |||||||
Db          1 LVFFAED 7


RESULT 10
US-08-986-948-11
; Sequence 11, Application US/08986948
; Patent No. 5955317
;  GENERAL INFORMATION:
;    APPLICANT:  SUZUKI, No. 5955317uhiro
;    APPLICANT:  ODAKA, Asano
;    APPLICANT:  KITADA, Chieko
;    TITLE OF INVENTION:  ANTIBODIES TO B-AMYLOIDS OR THEIR
;    TITLE OF INVENTION:  DERIVATIVES AND USE THEREOF
;    NUMBER OF SEQUENCES:  14
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  DIKE, BRONSTEIN, ROBERTS & CUSHMAN
;      STREET:  130 WATER STREET
;      CITY:  BOSTON
;      STATE:  MA
;      COUNTRY:  USA
;      ZIP:  02019
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Diskette
;      COMPUTER:  IBM Compatible
;      OPERATING SYSTEM:  DOS
;      SOFTWARE:  FastSEQ Version 1.5
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/986,948
;      FILING DATE:
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/302,808
;      FILING DATE:  15-SEP-1994
;      APPLICATION NUMBER:  PCT/JP94/00089
;      FILING DATE:  24-JAN-1994
;      APPLICATION NUMBER:  010132/1993
;      FILING DATE:  25-JAN-1993
;      APPLICATION NUMBER:  019035/1993
;      FILING DATE:  05-FEB-1993
;      APPLICATION NUMBER:  286985/1993
;      FILING DATE:  16-NOV-1993
;      APPLICATION NUMBER:  334773/1993
;      FILING DATE:  28-DEC-1993
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  DAVID, RESNICK S
;      REGISTRATION NUMBER:  34,235
;      REFERENCE/DOCKET NUMBER:  44631
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  617-523-3400
;      TELEFAX:  617-523-6440
;      TELEX:  200291 STRE
;  INFORMATION FOR SEQ ID NO:  11:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  12 amino acids
;      TYPE:  amino acid
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;       STRANDEDNESS:  single
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
;     HYPOTHETICAL:  NO
;     ANTI-SENSE:  NO
;     FRAGMENT TYPE:  N-terminal
;     ORIGINAL SOURCE:
US-08-986-948-11

  Query Match             85.4%;  Score 35;  DB 2;  Length 12;
  Best Local Similarity   100.0%;  Pred. No. 0.51;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          1 LVFFAED 7


RESULT 11
US-09-458-481B-13
; Sequence 13, Application US/09458481B
; Patent No. 6310048
; GENERAL INFORMATION:
;  APPLICANT: KUMAR, Vijaya B.
;  TITLE OF INVENTION: ANTISENSE MODULATION OF AMYLOID BETA PROTEIN EXPRESSION
;  FILE REFERENCE: 16153-9250
;  CURRENT APPLICATION NUMBER: US/09/458,481B
;  CURRENT FILING DATE:  1999-12-09
;  NUMBER OF SEQ ID NOS: 20
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 13
;   LENGTH: 14
;   TYPE: PRT
;   ORGANISM: Homo sapiens
;   FEATURE:
;   OTHER INFORMATION: Description of Artificial Sequence: Amino Acids
;   OTHER INFORMATION: Corresponding to Antisense Oligonucleotide
US-09-458-481B-13

  Query Match             85.4%;  Score 35;  DB 4;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 0.6;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          1 LVFFAED 7


RESULT 12
US-09-594-366-5
; Sequence 5, Application US/09594366
; Patent No. 6582945
; GENERAL INFORMATION:
;  APPLICANT: Raso, Victor
;  TITLE OF INVENTION: IMMUNOLOGICAL CONTROL OF BETA-AMYLOID LEVELS IN VIVO
;  FILE REFERENCE: BBRI-2004
;  CURRENT APPLICATION NUMBER: US/09/594,366
```

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;  CURRENT FILING DATE:  2000-06-15
;  PRIOR APPLICATION NUMBER: 60/139,408
;  PRIOR FILING DATE: 1999-06-16
;  NUMBER OF SEQ ID NOS: 7
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 5
;   LENGTH: 14
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-594-366-5

  Query Match             85.4%;  Score 35;  DB 4;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 0.6;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          5 LVFFAED 11


RESULT 13
US-08-612-785B-14
; Sequence 14, Application US/08612785B
; Patent No. 5854204
;  GENERAL INFORMATION:
;    APPLICANT:  Findeis, Mark A. et al.
;    TITLE OF INVENTION:  Ab Peptides that Modulate b-Amyloid
;    TITLE OF INVENTION:  Aggregation
;    NUMBER OF SEQUENCES:  40
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  28 State Street, Suite 510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/612,785B
;      FILING DATE:  Herewith
;      CLASSIFICATION:  514
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 08/404,831
;      FILING DATE:  14-MAR-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 08/475,579
;      FILING DATE:  07-JUN-1995
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  USSN 08/548,998
;      FILING DATE:  27-OCT-1995
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  DeConti, Giulio A.
;      REGISTRATION NUMBER:  31,503
```

```
;       REFERENCE/DOCKET NUMBER:  PPI-002CP3
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (617)227-7400
;       TELEFAX:  (617)742-4214
;   INFORMATION FOR SEQ ID NO:  14:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  15 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
;     FRAGMENT TYPE:  internal
US-08-612-785B-14

  Query Match             85.4%;  Score 35;  DB 2;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 0.65;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 14
US-08-612-785B-37
; Sequence 37, Application US/08612785B
; Patent No. 5854204
;  GENERAL INFORMATION:
;     APPLICANT:  Findeis, Mark A. et al.
;     TITLE OF INVENTION:  Ab Peptides that Modulate b-Amyloid
;     TITLE OF INVENTION:  Aggregation
;     NUMBER OF SEQUENCES:  40
;     CORRESPONDENCE ADDRESS:
;       ADDRESSEE:  LAHIVE & COCKFIELD
;       STREET:  28 State Street, Suite 510
;       CITY:  Boston
;       STATE:  Massachusetts
;       COUNTRY:  USA
;       ZIP:  02109-1875
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/612,785B
;       FILING DATE:  Herewith
;       CLASSIFICATION:  514
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/404,831
;       FILING DATE:  14-MAR-1995
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/475,579
;       FILING DATE:  07-JUN-1995
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/548,998
;       FILING DATE:  27-OCT-1995
;     ATTORNEY/AGENT INFORMATION:
```

```
;       NAME:  DeConti, Giulio A.
;       REGISTRATION NUMBER:  31,503
;       REFERENCE/DOCKET NUMBER:  PPI-002CP3
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (617)227-7400
;       TELEFAX:  (617)742-4214
;   INFORMATION FOR SEQ ID NO:  37:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  15 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
;     FRAGMENT TYPE:  internal
US-08-612-785B-37

  Query Match             85.4%;  Score 35;  DB 2;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 0.65;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          7 LVFFAED 13


RESULT 15
US-08-617-267C-14
; Sequence 14, Application US/08617267C
; Patent No. 6319498
;  GENERAL INFORMATION:
;     APPLICANT:  Findeis, Mark A. et al.
;     TITLE OF INVENTION:  Modulators of Amyloid Aggregation
;     NUMBER OF SEQUENCES:  45
;     CORRESPONDENCE ADDRESS:
;       ADDRESSEE:  LAHIVE & COCKFIELD, LLP
;       STREET:  28 State Street
;       CITY:  Boston
;       STATE:  Massachusetts
;       COUNTRY:  USA
;       ZIP:  02109-1875
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/617,267C
;       FILING DATE:  14-MAR-1996
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/404,831
;       FILING DATE:  14-MAR-1995
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/475,579
;       FILING DATE:  07-JUN-1995
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  USSN 08/548,998
;       FILING DATE:  27-OCT-1995
;     ATTORNEY/AGENT INFORMATION:
```

; NAME: DeConti, Giulio A.
; REGISTRATION NUMBER: 31,503
; REFERENCE/DOCKET NUMBER: PPI-002CP2
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: (617)227-7400
; TELEFAX: (617)227-5941
; INFORMATION FOR SEQ ID NO: 14:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 15 amino acids
; TYPE: amino acid
; TOPOLOGY: linear
; MOLECULE TYPE: peptide
; FRAGMENT TYPE: internal
US-08-617-267C-14

Query Match 85.4%; Score 35; DB 4; Length 15;
Best Local Similarity 100.0%; Pred. No. 0.65;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8
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Search completed: March 4, 2004, 15:42:14
Job time : 0.519149 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 4, 2004, 15:30:05 ; Search time 0.434043 Seconds
(without alignments)
1772.942 Million cell updates/sec

Title: US-09-668-314C-84
Perfect score: 41
Sequence: 1 LVFFAEDF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 283366 seqs, 96191526 residues

Total number of hits satisfying chosen parameters: 283366

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : PIR_78:*
1: pir1:*
2: pir2:*
3: pir3:*
4: pir4:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	35	85.4	33	2	S23094	beta-amyloid prote
2	35	85.4	42	2	PN0512	beta-amyloid prote
3	35	85.4	57	2	E60045	Alzheimer's diseas
4	35	85.4	57	2	F60045	Alzheimer's diseas
5	35	85.4	57	2	G60045	Alzheimer's diseas
6	35	85.4	57	2	D60045	Alzheimer's diseas
7	35	85.4	57	2	A60045	Alzheimer's diseas
8	35	85.4	57	2	B60045	Alzheimer's diseas
9	35	85.4	82	2	PQ0438	Alzheimer's diseas
10	35	85.4	695	1	A49795	Alzheimer's diseas
11	35	85.4	695	2	A27485	Alzheimer's diseas
12	35	85.4	695	2	S00550	Alzheimer's diseas
13	35	85.4	770	1	QRHUA4	Alzheimer's diseas

14	33	80.5	222	2	T24151	hypothetical prote
15	33	80.5	455	2	D69078	probable phosphoma
16	33	80.5	502	2	T27908	hypothetical prote
17	32	78.0	261	2	B89868	conserved hypothet
18	32	78.0	398	2	T44331	hypothetical prote
19	31	75.6	150	2	T29939	hypothetical prote
20	31	75.6	182	2	T35807	hypothetical prote
21	31	75.6	224	2	G71483	hypothetical prote
22	31	75.6	291	2	AB1397	hypothetical prote
23	31	75.6	301	2	S39679	transcription regu
24	31	75.6	368	2	F70327	conserved hypothet
25	31	75.6	582	2	I38028	matrix metalloprot
26	31	75.6	614	2	T40652	hypothetical prote
27	31	75.6	622	2	T24632	hypothetical prote
28	31	75.6	741	2	T46488	hypothetical prote
29	31	75.6	747	2	JH0773	Alzheimer's diseas
30	31	75.6	1364	2	T51920	probable xanthine
31	30	73.2	174	2	AC1587	hypothetical prote
32	30	73.2	216	2	T12812	hypothetical prote
33	30	73.2	222	2	T32121	hypothetical prote
34	30	73.2	224	2	E72049	conserved hypothet
35	30	73.2	224	2	F86575	CT691 hypothetical
36	30	73.2	258	2	AG0459	Sec-independent pr
37	30	73.2	327	2	F83773	ABC transporter (s
38	30	73.2	402	2	B90519	hypothetical prote
39	30	73.2	457	2	AF0003	oxygen-independent
40	30	73.2	471	2	T47568	fructokinase-like
41	30	73.2	566	2	S54091	hypothetical prote
42	30	73.2	582	2	T46822	phytoene desaturas
43	30	73.2	641	2	H69651	lichenan operon tr
44	30	73.2	664	2	D81330	glycine-tRNA ligas
45	30	73.2	745	2	T03119	hypothetical prote

ALIGNMENTS

RESULT 1
S23094
beta-amyloid protein precursor - rat
C;Species: Rattus norvegicus (Norway rat)
C;Date: 22-Nov-1993 #sequence_revision 10-Nov-1995 #text_change 03-May-1996
C;Accession: S23094
R;Kojima, S.; Omori, M.
FEBS Lett. 304, 57-60, 1992
A;Title: Two-way cleavage of beta-amyloid protein precursor by multicatalytic proteinase.
A;Reference number: S23094; MUID:92316198; PMID:1618299
A;Accession: S23094
A;Molecule type: protein
A;Residues: 1-33 <KOJ>
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology

Query Match 85.4%; Score 35; DB 2; Length 33;
Best Local Similarity 100.0%; Pred. No. 0.95;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
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RESULT 2
PN0512
beta-amyloid protein - guinea pig (fragment)
C;Species: Cavia porcellus (guinea pig)
C;Date: 31-Dec-1993 #sequence_revision 31-Dec-1993 #text_change 17-Mar-1999
C;Accession: PN0512
R;Shimohigashi, Y.; Matsumoto, H.; Takano, Y.; Saito, R.; Iwata, T.; Kamiya, H.; Ohno, M.
Biochem. Biophys. Res. Commun. 193, 624-630, 1993
A;Title: Receptor-mediated specific biological activity of a beta-amyloid protein fragment for NK-1 substance p receptors.
A;Reference number: PN0512; MUID:93290653; PMID:7685598
A;Accession: PN0512
A;Molecule type: protein
A;Residues: 1-42 <SHI>
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid

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  Query Match             85.4%;  Score 35;  DB 2;  Length 42;
  Best Local Similarity   100.0%;  Pred. No. 1.2;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         17 LVFFAED 23
```

RESULT 3
E60045
Alzheimer's disease amyloid beta/A4 protein precursor - sheep (fragment)
C;Species: Ovis sp. (sheep)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: E60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: E60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56130
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

```
  Query Match             85.4%;  Score 35;  DB 2;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 1.7;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
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```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
```

RESULT 4
F60045
Alzheimer's disease amyloid beta/A4 protein precursor - pig (fragment)
C;Species: Sus scrofa domestica (domestic pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: F60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: F60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56127; NID:g1895; PIDN:CAA39592.1; PID:g1896
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 85.4%; Score 35; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 1.7;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
```

RESULT 5
G60045
Alzheimer's disease amyloid beta/A4 protein precursor - guinea pig (fragment)
C;Species: Cavia porcellus (guinea pig)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: G60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: G60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56126
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 85.4%; Score 35; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 1.7;

Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
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RESULT 6
D60045
Alzheimer's disease amyloid beta/A4 protein precursor - bovine (fragment)
C;Species: Bos primigenius taurus (cattle)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: D60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: D60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56124
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 85.4%; Score 35; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 1.7;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
```

RESULT 7
A60045
Alzheimer's disease amyloid beta/A4 protein precursor - dog (fragment)
C;Species: Canis lupus familiaris (dog)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 28-Jul-1995
C;Accession: A60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: A60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56125
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 85.4%; Score 35; DB 2; Length 57;

Best Local Similarity 100.0%; Pred. No. 1.7;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
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RESULT 8
B60045
Alzheimer's disease amyloid beta/A4 protein precursor - polar bear (fragment)
C;Species: Ursus maritimus (polar bear)
C;Date: 01-Dec-1992 #sequence_revision 01-Dec-1992 #text_change 13-Aug-1999
C;Accession: B60045
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.
A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: B60045
A;Molecule type: mRNA
A;Residues: 1-57 <JOH>
A;Cross-references: EMBL:X56128; NID:g2165; PIDN:CAA39593.1; PID:g2166
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; brain

Query Match 85.4%; Score 35; DB 2; Length 57;
Best Local Similarity 100.0%; Pred. No. 1.7;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28
```

RESULT 9
PQ0438
Alzheimer's disease amyloid A4 protein precursor - rabbit (fragment)
C;Species: Oryctolagus cuniculus (domestic rabbit)
C;Date: 30-Sep-1993 #sequence_revision 19-Oct-1995 #text_change 19-Oct-1995
C;Accession: PQ0438; C60045
R;Davidson, J.S.; West, R.L.; Kotikalapudi, P.; Maroun, L.E.
Biochem. Biophys. Res. Commun. 188, 905-911, 1992
A;Title: Sequence and methylation in the beta/A4 region of the rabbit amyloid precursor protein gene.
A;Reference number: PQ0438; MUID:93075180; PMID:1445331
A;Accession: PQ0438
A;Molecule type: DNA
A;Residues: 1-82 <DAV>
A;Cross-references: GB:M83558; GB:M83657
R;Johnstone, E.M.; Chaney, M.O.; Norris, F.H.; Pascual, R.; Little, S.P.
Brain Res. Mol. Brain Res. 10, 299-305, 1991
A;Title: Conservation of the sequence of the Alzheimer's disease amyloid peptide in dog, polar bear and five other mammals by cross-species polymerase chain reaction analysis.

A;Reference number: A60045; MUID:92017079; PMID:1656157
A;Accession: C60045
A;Molecule type: mRNA
A;Residues: 12-68 <JOH>
A;Cross-references: EMBL:X56129
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; Alzheimer's disease; amyloid; Down's syndrome

  Query Match 85.4%; Score 35; DB 2; Length 82;
  Best Local Similarity 100.0%; Pred. No. 2.4;
  Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
      |||||||
Db 33 LVFFAED 39

RESULT 10
A49795
Alzheimer's disease amyloid beta protein precursor - crab-eating macaque
C;Species: Macaca fascicularis (crab-eating macaque)
C;Date: 10-Sep-1999 #sequence_revision 10-Sep-1999 #text_change 10-Sep-1999
C;Accession: A49795
R;Podlisny, M.B.; Tolan, D.R.; Selkoe, D.J.
Am. J. Pathol. 138, 1423-1435, 1991
A;Title: Homology of the amyloid beta protein precursor in monkey and human supports a primate model for beta amyloidosis in Alzheimer's disease.
A;Reference number: A49795; MUID:91273117; PMID:1905108
A;Accession: A49795
A;Status: preliminary
A;Molecule type: mRNA
A;Residues: 1-695 <POD>
A;Cross-references: GB:M58727; NID:g342062; PIDN:AAA36829.1; PID:g342063
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing

  Query Match 85.4%; Score 35; DB 1; Length 695;
  Best Local Similarity 100.0%; Pred. No. 22;
  Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
      |||||||
Db 613 LVFFAED 619

RESULT 11
A27485
Alzheimer's disease amyloid beta/A4 protein homolog precursor - mouse
N;Alternate names: proteinase nexin II
C;Species: Mus musculus (house mouse)
C;Date: 31-Mar-1989 #sequence_revision 31-Mar-1989 #text_change 13-Aug-1999
C;Accession: A27485; S19727; I49485
R;Yamada, T.; Sasaki, H.; Furuya, H.; Miyata, T.; Goto, I.; Sakaki, Y.
Biochem. Biophys. Res. Commun. 149, 665-671, 1987

A;Title: Complementary DNA for the mouse homolog of the human amyloid beta protein precursor.
A;Reference number: A27485; MUID:88106489; PMID:3322280
A;Accession: A27485
A;Molecule type: mRNA
A;Residues: 1-695 <YAM>
A;Cross-references: GB:M18373; NID:g191568; PIDN:AAA37139.1; PID:g309085
A;Experimental source: brain
R;de Strooper, B.; van Leuven, F.; van den Berghe, H.
Biochim. Biophys. Acta 1129, 141-143, 1991
A;Title: The amyloid beta protein precursor or proteinase nexin II from mouse is closer related to its human homolog than previously reported.
A;Reference number: S19727; MUID:92096458; PMID:1756177
A;Accession: S19727
A;Molecule type: mRNA
A;Residues: 1-210,'G',212-220,'S',222-396,'A',398-402,'T',404-448,'A',450-695 <STR>
A;Cross-references: EMBL:X59379
R;Izumi, R.; Yamada, T.; Yoshikai, S.; Sasaki, H.; Hattori, M.; Sakaki, Y.
Gene 112, 189-195, 1992
A;Title: Positive and negative regulatory elements for the expression of the Alzheimer's disease amyloid precursor-encoding gene in mouse.
A;Reference number: I49485; MUID:92209998; PMID:1555768
A;Accession: I49485
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-19 <RES>
A;Cross-references: GB:D10603; NID:g220328; PIDN:BAA01456.1; PID:g220329
C;Genetics:
A;Map position: 16C3
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; transmembrane protein

  Query Match 85.4%; Score 35; DB 2; Length 695;
  Best Local Similarity 100.0%; Pred. No. 22;
  Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
      |||||||
Db 613 LVFFAED 619

RESULT 12
S00550
Alzheimer's disease amyloid beta protein precursor - rat
N;Alternate names: beta-A4 amyloid protein
C;Species: Rattus norvegicus (Norway rat)
C;Date: 30-Jun-1989 #sequence_revision 30-Jun-1989 #text_change 13-Aug-1999
C;Accession: S00550; A41245; A39820; S46251
R;Shivers, B.D.; Hilbich, C.; Multhaup, G.; Salbaum, M.; Beyreuther, K.; Seeburg, P.H.
EMBO J. 7, 1365-1370, 1988
A;Title: Alzheimer's disease amyloidogenic glycoprotein: expression pattern in rat brain suggests a role in cell contact.
A;Reference number: S00550; MUID:88312583; PMID:2900758
A;Accession: S00550

A;Molecule type: mRNA
A;Residues: 1-695 <SHI>
A;Cross-references: EMBL:X07648; NID:g55616; PIDN:CAA30488.1; PID:g55617
R;Schubert, D.; Schroeder, R.; LaCorbiere, M.; Saitoh, T.; Cole, G.
Science 241, 223-226, 1988
A;Title: Amyloid beta protein precursor is possibly a heparan sulfate proteoglycan core protein.
A;Reference number: A41245; MUID:88264430; PMID:2968652
A;Accession: A41245
A;Molecule type: protein
A;Residues: 18-37,'X',39-40,'X',42-44 <SCH>
A;Note: evidence for heparan sulfate attachment
R;Hesse, L.; Beher, D.; Masters, C.L.; Multhaup, G.
FEBS Lett. 349, 109-116, 1994
A;Title: The beta-A4 amyloid precursor protein binding to copper.
A;Reference number: S46251; MUID:94320627; PMID:7913895
A;Contents: annotation; copper binding sites
A;Note: rat peptides were isolated but not sequenced
R;Potempska, A.; Styles, J.; Mehta, P.; Kim, K.S.; Miller, D.L.
J. Biol. Chem. 266, 8464-8469, 1991
A;Title: Purification and tissue level of the beta-amyloid peptide precursor of rat brain.
A;Reference number: A39820; MUID:91217087; PMID:1673681
A;Accession: A39820
A;Status: preliminary
A;Molecule type: protein
A;Residues: 18-32 <POT>
A;Experimental source: brain
C;Comment: Deposition of amyloid protein as neurofibrillary tangles and/or plaques is characteristic of both Alzheimer's disease and Down's syndrome.
C;Superfamily: Alzheimer's disease amyloid beta protein; animal Kunitz-type proteinase inhibitor homology
C;Keywords: alternative splicing; amyloid; glycoprotein; transmembrane protein
F;625-648/Domain: transmembrane #status predicted <TMM>

  Query Match 85.4%; Score 35; DB 2; Length 695;
  Best Local Similarity 100.0%; Pred. No. 22;
  Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 LVFFAED 7
      |||||||
Db 613 LVFFAED 619

RESULT 13
QRHUA4
Alzheimer's disease amyloid beta protein precursor [validated] - human
N;Alternate names: Alzheimer's disease amyloid A4 protein; coagulation factor XIa inhibitor; proteinase nexin II (PN-II)
N;Contains: amyloid beta protein long, plaque form; amyloid beta protein short, vascular form; amyloid protein precursor splice form APP(695); amyloid protein precursor splice form APP(751); amyloid protein precursor splice form APP(770)
C;Species: Homo sapiens (man)
C;Date: 30-Jun-1987 #sequence_revision 28-Jul-1995 #text_change 15-Sep-2000
C;Accession: S02260; S05194; A32277; A33260; A35486; I39452; I39451; I39453; I59562; A44017; B44017; A03134; A29030; A47584; A47585; S02638; S00707; S00925; A38949; A30320; B30320; C30320; A31087; A24668; A28583; A29302; A60805; JL0038;

S06121; A60355; A59011; A38384; S29076; S38252; S32539; S48148; S48692; S51186; S51185; S51184; S51183; A54238; I58075; I52250; S09010; S10737; S24127; S43644
R;Lemaire, H.G.; Salbaum, J.M.; Multhaup, G.; Kang, J.; Bayney, R.M.; Unterbeck, A.; Beyreuther, K.; Mueller-Hill, B.
Nucleic Acids Res. 17, 517-522, 1989
A;Title: The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid is encoded by 16 exons.
A;Reference number: S02260; MUID:89128427; PMID:2783775
A;Accession: S02260
A;Molecule type: DNA
A;Residues: 1-288,'V',365-770 <LEM1>
A;Cross-references: EMBL:X13466
A;Note: alternative splice form APP(695)
R;Lemaire, H.G.
submitted to the EMBL Data Library, November 1988
A;Reference number: S05194
A;Accession: S05194
A;Molecule type: DNA
A;Residues: 1-14,'VW',17-288,'V',365-770 <LEM2>
A;Cross-references: EMBL:X13466; NID:g35598; PIDN:CAA31830.1; PID:g871360
A;Note: alternative splice form APP(695)
R;La Fauci, G.; Lahiri, D.K.; Salton, S.R.J.; Robakis, N.K.
Biochem. Biophys. Res. Commun. 159, 297-304, 1989
A;Title: Characterization of the 5'-end region and the first two exons of the beta-protein precursor gene.
A;Reference number: A32277; MUID:89165870; PMID:2538123
A;Accession: A32277
A;Molecule type: DNA
A;Residues: 1-75 <LAF>
A;Cross-references: GB:M24546; GB:M24547; NID:g341202; PIDN:AAC13654.1; PID:g516074
R;Johnstone, E.M.; Chaney, M.O.; Moore, R.E.; Ward, K.E.; Norris, F.H.; Little, S.P.
Biochem. Biophys. Res. Commun. 163, 1248-1255, 1989
A;Title: Alzheimer's disease amyloid peptide is encoded by two exons and shows similarity to soybean trypsin inhibitor.
A;Reference number: A33260; MUID:89392030; PMID:2675837
A;Accession: A33260
A;Molecule type: DNA
A;Residues: 656-737 <JOH>
A;Cross-references: GB:M29270; NID:g178863; PIDN:AAA51768.1; PID:g178865
R;Prelli, F.; Levy, E.; van Duinen, S.G.; Bots, G.T.A.M.; Luyendijk, W.; Frangione, B.
Biochem. Biophys. Res. Commun. 170, 301-307, 1990
A;Title: Expression of a normal and variant Alzheimer's beta-protein gene in amyloid of hereditary cerebral hemorrhage, Dutch type: DNA and protein diagnostic assays.
A;Reference number: A35486; MUID:90321244; PMID:2196878
A;Accession: A35486
A;Molecule type: DNA
A;Residues: 672-710 <PRE1>
A;Note: 693-Gln was found in DNA isolated from HCHWA-D patients
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 87, 257-263, 1990
A;Title: Genomic organization of the human amyloid beta-protein precursor gene.
A;Reference number: I39451; MUID:90236318; PMID:2110105
A;Accession: I39452

A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-770 <YOS1>
A;Cross-references: GB:M33112; NID:g178613; PIDN:AAB59502.1; PID:g178616
A;Accession: I39451
A;Status: nucleic acid sequence not shown; translation not shown; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-530,'QWLMPVIPAFWEAKVGR' <YOS2>
A;Cross-references: GB:M34875; NID:g178608; PIDN:AAB59501.1; PID:g178615
R;Yoshikai, S.I.; Sasaki, H.; Doh-ura, K.; Furuya, H.; Sakaki, Y.
Gene 102, 291-292, 1991
A;Reference number: A59020; MUID:91340168; PMID:1908403
A;Contents: annotation; erratum
A;Note: revised physical map for reference I39451
R;Levy, E.; Carman, M.D.; Fernandez-Madrid, I.J.; Power, M.D.; Lieberburg, I.; van Duinen, S.G.; Bots, G.T.; Luyendijk, W.; Frangione, B.
Science 248, 1124-1126, 1990
A;Title: Mutation of the Alzheimer's disease amyloid gene in hereditary cerebral hemorrhage, Dutch type.
A;Reference number: I39453; MUID:90260663; PMID:2111584
A;Accession: I39453
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 656-737 <LEV>
A;Cross-references: GB:M37896; NID:g178618; PIDN:AAA51727.1; PID:g178620
A;Note: a mutation with 693-Gln is presented
R;Murrell, J.; Farlow, M.; Ghetti, B.; Benson, M.D.
Science 254, 97-99, 1991
A;Title: A mutation in the amyloid precursor protein associated with hereditary Alzheimer's disease.
A;Reference number: I59562; MUID:92022553; PMID:1925564
A;Accession: I59562
A;Status: translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 689-716,'F',718-737 <MUR>
A;Cross-references: GB:S57665; NID:g236720; PIDN:AAB19991.1; PID:g236721
R;Kamino, K.; Orr, H.T.; Payami, H.; Wijsman, E.M.; Alonso, M.E.; Pulst, S.M.; Anderson, L.; O'dahl, S.; Nemens, E.; White, J.A.; Sadovnick, A.D.; Ball, M.J.; Kaye, J.; Warren, A.; McInnis, M.; Antonarakis, S.E.; Korenberg, J.R.; Sharma, V.; Kukull, W.; Larson, E.; Heston, L.L.; Martin, G.M.; Bird, T.D.; Schellenberg, G.D.
Am. J. Hum. Genet. 51, 998-1014, 1992
A;Title: Linkage and mutational analysis of familial Alzheimer disease kindreds for the APP gene region.
A;Reference number: A44017; MUID:93035397; PMID:1415269
A;Accession: A44017
A;Molecule type: DNA
A;Residues: 687-692,'G',694-718 <KAM1>
A;Cross-references: GB:S45135; NID:g257377; PIDN:AAB23645.1; PID:g257378
A;Experimental source: familial Alzheimer disease family SB
A;Note: sequence extracted from NCBI backbone (NCBIP:115374)
A;Accession: B44017
A;Molecule type: DNA
A;Residues: 687-718 <KAM2>
A;Cross-references: GB:S45136; NID:g257379; PIDN:AAB23646.1; PID:g257380

A;Experimental source: familial Alzheimer disease family LIT
A;Note: sequence extracted from NCBI backbone (NCBIP:115376)
A;Note: this sequence has a silent mutation
R;Kang, J.; Lemaire, H.G.; Unterbeck, A.; Salbaum, J.M.; Masters, C.L.; Grzeschik, K.H.; Multhaup, G.; Beyreuther, K.; Muller-Hill, B.
Nature 325, 733-736, 1987
A;Title: The precursor of Alzheimer's disease amyloid A4 protein resembles a cell-surface receptor.
A;Reference number: A03134; MUID:87144572; PMID:2881207
A;Accession: A03134
A;Molecule type: mRNA
A;Residues: 1-288,'V',365-770 <KAN>
A;Cross-references: GB:Y00264; NID:g28525; PIDN:CAA68374.1; PID:g28526
A;Note: alternative splice form APP(695)
R;Robakis, N.K.; Ramakrishna, N.; Wolfe, G.; Wisniewski, H.M.
Proc. Natl. Acad. Sci. U.S.A. 84, 4190-4194, 1987
A;Title: Molecular cloning and characterization of a cDNA encoding the cerebrovascular and the neuritic plaque amyloid peptides.
A;Reference number: A29030; MUID:87231971; PMID:3035574
A;Accession: A29030
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-646,'E',648-770 <ROB>
A;Cross-references: GB:M16765; NID:g178539; PIDN:AAA51722.1; PID:g178540
A;Note: the authors translated the codon GAG for residue 647 as Asp
R;Goldgaber, D.; Lerman, M.I.; McBride, O.W.; Saffiotti, U.; Gajdusek, D.C.
Science 235, 877-880, 1987
A;Title: Characterization and chromosomal localization of a cDNA encoding brain amyloid of Alzheimer's disease.
A;Reference number: A47584; MUID:87120328; PMID:3810169
A;Accession: A47584
A;Molecule type: mRNA
A;Residues: 674-756,'S',758-770 <GOL>
A;Cross-references: GB:M15533; NID:g178706; PIDN:AAA35540.1; PID:g178707
A;Experimental source: brain
R;Tanzi, R.E.; Gusella, J.F.; Watkins, P.C.; Bruns, G.A.P.; St George-Hyslop, P.; Van Keuren, M.L.; Patterson, D.; Pagan, S.; Kurnit, D.M.; Neve, R.L.
Science 235, 880-884, 1987
A;Title: Amyloid beta protein gene: cDNA, mRNA distribution, and genetic linkage near the Alzheimer locus.
A;Reference number: A47585; MUID:87120329; PMID:2949367
A;Accession: A47585
A;Molecule type: mRNA
A;Residues: 674-703 <TAN1>
A;Cross-references: GB:M15532; NID:g177957; PIDN:AAA51564.1; PID:g177958
R;Dyrks, T.; Weidemann, A.; Multhaup, G.; Salbaum, J.M.; Lemaire, H.G.; Kang, J.; Mueller-Hill, B.; Masters, C.L.; Beyreuther, K.
EMBO J. 7, 949-957, 1988
A;Title: Identification, transmembrane orientation and biogenesis of the amyloid A4 precursor of Alzheimer's disease.
A;Reference number: S02638; MUID:88296437; PMID:2900137
A;Accession: S02638
A;Molecule type: mRNA
A;Residues: 672-678 <DYR>
R;Tanzi, R.E.; McClatchey, A.I.; Lamperti, E.D.; Villa-Komaroff, L.; Gusella, J.F.; Neve, R.L.
Nature 331, 528-530, 1988

A;Title: Protease inhibitor domain encoded by an amyloid protein precursor mRNA associated with Alzheimer's disease.
A;Reference number: S00707; MUID:88122640; PMID:2893290
A;Accession: S00707
A;Molecule type: mRNA
A;Residues: 286-344,'I',365-366 <TAN2>
A;Cross-references: EMBL:X06982; NID:g28817; PIDN:CAA30042.1; PID:g929612
A;Experimental source: promyelocytic leukemia cell line HL60
A;Note: alternative splice form APP(751)
R;Ponte, P.; Gonzalez-DeWhitt, P.; Schilling, J.; Miller, J.; Hsu, D.; Greenberg, B.; Davis, K.; Wallace, W.; Lieberburg, I.; Fuller, F.; Cordell, B.
Nature 331, 525-527, 1988
A;Title: A new A4 amyloid mRNA contains a domain homologous to serine proteinase inhibitors.
A;Reference number: S00925; MUID:88122639; PMID:2893289
A;Accession: S00925
A;Molecule type: mRNA
A;Residues: 1-344,'I',365-770 <PO2>
A;Cross-references: GB:X06989; EMBL:Y00297; NID:g28720; PIDN:CAA30050.1; PID:g28721
A;Note: alternative splice form APP(751)
R;Kitaguchi, N.; Takahashi, Y.; Tokushima, Y.; Shiojiri, S.; Ito, H.
Nature 331, 530-532, 1988
A;Title: Novel precursor of Alzheimer's disease amyloid protein shows protease inhibitory activity.
A;Reference number: A38949; MUID:88122641; PMID:2893291
A;Accession: A38949
A;Molecule type: mRNA
A;Residues: 287-367 <KIT>
A;Cross-references: GB:X06981; NID:g28816; PIDN:CAA30041.1; PID:g929611
A;Experimental source: glioblastoma cell line
A;Note: alternative splice form APP(770)
R;Vitek, M.P.; Rasool, C.G.; de Sauvage, F.; Vitek, S.M.; Bartus, R.T.; Beer, B.; Ashton, R.A.; Macq, A.F.; Maloteaux, J.M.; Blume, A.J.; Octave, J.N.
Brain Res. Mol. Brain Res. 4, 121-131, 1988
A;Title: Absence of mutation in the beta-amyloid cDNAs cloned from the brains of three patients with sporadic Alzheimer's disease.
A;Reference number: A30320
A;Accession: A30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 284-288,'V',365-770 <VIT1>
A;Accession: B30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 122-288,'V',365-770 <VIT2>
A;Accession: C30320
A;Status: not compared with conceptual translation
A;Molecule type: mRNA
A;Residues: 606-770 <VIT3>
R;Zain, S.B.; Salim, M.; Chou, W.G.; Sajdel-Sulkowska, E.M.; Majocha, R.E.; Marotta, C.A.
Proc. Natl. Acad. Sci. U.S.A. 85, 929-933, 1988
A;Title: Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer disease brain: coding and noncoding regions of the fetal precursor mRNA are expressed in the cortex.
A;Reference number: A31087; MUID:88124954; PMID:2893379

A;Accession: A31087
A;Molecule type: mRNA
A;Residues: 507-770 <ZAI>
A;Cross-references: GB:M18734; NID:g178572; PIDN:AAA51726.1; PID:g178573
A;Note: the authors translated the codon GAA for residue 599 as Gly, ACC for residue 603 as Val, GTG for residue 604 as Glu, GAG for residue 605 as Leu, CTT for residue 607 as Pro, CCC for residue 608 as Val, GTG for residue 609 as Asn, AAT for residue 610 as Gly, and GGT for residue 655 as Ser
A;Note: the cited Genbank accession number, J03594, is not in release 101.0
R;Masters, C.L.; Multhaup, G.; Simms, G.; Pottgiesser, J.; Martins, R.N.; Beyreuther, K.

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Db 688 LVFFAED 694

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C;Species: Caenorhabditis elegans
C;Date: 15-Oct-1999 #sequence_revision 15-Oct-1999 #text_change 15-Oct-1999
C;Accession: T24151
R;Bardill, S.
submitted to the EMBL Data Library, April 1996
A;Reference number: Z19846
A;Accession: T24151
A;Status: preliminary; translated from GB/EMBL/DDBJ
A;Molecule type: DNA
A;Residues: 1-222 <WIL>
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A;Map position: 4
A;Introns: 13/1; 34/1; 60/2

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RESULT 15
D69078
probable phosphomannomutase 2 - Methanobacterium thermoautotrophicum (strain Delta H)
C;Species: Methanobacterium thermoautotrophicum
C;Date: 05-Dec-1997 #sequence_revision 05-Dec-1997 #text_change 17-Mar-2000
C;Accession: D69078

R;Smith, D.R.; Doucette-Stamm, L.A.; Deloughery, C.; Lee, H.; Dubois, J.; Aldredge, T.; Bashirzadeh, R.; Blakely, D.; Cook, R.; Gilbert, K.; Harrison, D.; Hoang, L.; Keagle, P.; Lumm, W.; Pothier, B.; Qiu, D.; Spadafora, R.; Vicaire, R.; Wang, Y.; Wierzbowski, J.; Gibson, R.; Jiwani, N.; Caruso, A.; Bush, D.; Safer, H.; Patwell, D.; Prabhakar, S.; McDougall, S.; Shimer, G.; Goyal, A.; Pietrokovski, S.; Church, G.M.; Daniels, C.J.; Mao, J.; Rice, P.; Noelling, J.; Reeve, J.N.
J. Bacteriol. 179, 7135-7155, 1997
A;Title: Complete genome sequence of Methanobacterium thermoautotrophicum Delta H: functional analysis and comparative genomics.
A;Reference number: A69000; MUID:98037514; PMID:9371463
A;Accession: D69078
A;Status: preliminary; nucleic acid sequence not shown; translation not shown
A;Molecule type: DNA
A;Residues: 1-455 <MTH>
A;Cross-references: GB:AE000918; GB:AE000666; NID:g2622699; PIDN:AAB86057.1; PID:g2622707
A;Experimental source: strain Delta H
C;Genetics:
A;Gene: MTH1584
C;Superfamily: phosphomannomutase

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Job time : 1.43404 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

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(without alignments)
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Scoring table: BLOSUM62
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Searched: 809742 seqs, 211153259 residues

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Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

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1	35	85.4	8	14	US-10-235-483-1	Sequence 1, Appli
2	35	85.4	9	9	US-09-899-815-2	Sequence 2, Appli
3	35	85.4	9	14	US-10-235-483-64	Sequence 64, Appl
4	35	85.4	11	9	US-09-988-842-9	Sequence 9, Appli
5	35	85.4	11	9	US-09-988-842-25	Sequence 25, Appl
6	35	85.4	11	14	US-10-235-483-14	Sequence 14, Appl
7	35	85.4	13	14	US-10-281-458-1	Sequence 1, Appli
8	35	85.4	14	9	US-09-992-800-5	Sequence 5, Appli
9	35	85.4	14	9	US-09-992-994-5	Sequence 5, Appli
10	35	85.4	14	15	US-10-385-065-5	Sequence 5, Appli
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16	35	85.4	15	14	US-10-235-483-59	Sequence 59, Appl
17	35	85.4	15	14	US-10-235-483-63	Sequence 63, Appl
18	35	85.4	15	14	US-10-235-483-65	Sequence 65, Appl
19	35	85.4	15	15	US-10-463-729-14	Sequence 14, Appl
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27	35	85.4	28	9	US-09-867-847-4	Sequence 4, Appli
28	35	85.4	28	10	US-09-865-294-66	Sequence 66, Appl
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31	35	85.4	30	9	US-09-861-847-1	Sequence 1, Appli
32	35	85.4	30	14	US-10-301-488A-1	Sequence 1, Appli
33	35	85.4	33	10	US-09-930-915A-295	Sequence 295, App
34	35	85.4	33	14	US-10-082-014-84	Sequence 84, Appl
35	35	85.4	33	14	US-10-372-076-85	Sequence 85, Appl
36	35	85.4	35	9	US-09-867-847-3	Sequence 3, Appli
37	35	85.4	35	9	US-09-972-475-16	Sequence 16, Appl
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39	35	85.4	36	9	US-09-861-847-6	Sequence 6, Appli
40	35	85.4	36	9	US-09-861-847-11	Sequence 11, Appl
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45	35	85.4	40	9	US-09-861-847-7	Sequence 7, Appli

ALIGNMENTS

RESULT 1
US-10-235-483-1
; Sequence 1, Application US/10235483
; Publication No. US20030087407A1
; GENERAL INFORMATION:
; APPLICANT: SOTO-JARA, Claudio

```
;                    BAUMANN, Marc
;                    FRANGIONE, Blas
;         TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                             COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                             ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                             DEPOSITS
;         NUMBER OF SEQUENCES: 69
;         CORRESPONDENCE ADDRESS:
;              ADDRESSEE: BROWDY AND NEIMARK
;              STREET: 419 Seventh Street, N.W., Suite 400
;              CITY: Washington
;              STATE: D.C.
;              COUNTRY: USA
;              ZIP: 20004
;         COMPUTER READABLE FORM:
;              MEDIUM TYPE: Floppy disk
;              COMPUTER: IBM PC compatible
;              OPERATING SYSTEM: PC-DOS/MS-DOS
;              SOFTWARE: PatentIn Release #1.0, Version #1.30
;         CURRENT APPLICATION DATA:
;              APPLICATION NUMBER: US/10/235,483
;              FILING DATE: 06-Sep-2002
;              CLASSIFICATION: <Unknown>
;         PRIOR APPLICATION DATA:
;              APPLICATION NUMBER: US/08/766,596
;              FILING DATE: <Unknown>
;              APPLICATION NUMBER: US 08/630,645
;              FILING DATE: 10-APR-1996
;              APPLICATION NUMBER: US 08/478,326
;              FILING DATE: 06-JUN-1995
;         ATTORNEY/AGENT INFORMATION:
;              NAME: YUN, Allen C.
;              REGISTRATION NUMBER: 37,971
;              REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;         TELECOMMUNICATION INFORMATION:
;              TELEPHONE: 202-628-5197
;              TELEFAX: 202-737-3528
;    INFORMATION FOR SEQ ID NO: 1:
;         SEQUENCE CHARACTERISTICS:
;              LENGTH: 8 amino acids
;              TYPE: amino acid
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;              TOPOLOGY: linear
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;         SEQUENCE DESCRIPTION: SEQ ID NO: 1:
US-10-235-483-1

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  Best Local Similarity   100.0%;  Pred. No. 7.1e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8
```

```
RESULT 2
US-09-899-815-2
; Sequence 2, Application US/09899815
; Patent No. US20020162129A1
; GENERAL INFORMATION:
;  APPLICANT: LANNFELT, Lars
;  TITLE OF INVENTION: PREVENTION AND TREATMENT OF ALZHEIMER'S DISEASE
;  FILE REFERENCE: LANNFELT=1A
;  CURRENT APPLICATION NUMBER: US/09/899,815
;  CURRENT FILING DATE:  2001-07-09
;  PRIOR APPLICATION NUMBER: US 60/217,098
;  PRIOR FILING DATE: 2000-07-10
;  PRIOR APPLICATION NUMBER: EP 00202387.7
;  PRIOR FILING DATE: 2000-07-07
;  NUMBER OF SEQ ID NOS: 4
;  SOFTWARE: PatentIn version 3.1
; SEQ ID NO 2
;   LENGTH: 9
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: synthetic peptide  (16-24 of SEQ ID NO:1)
US-09-899-815-2

  Query Match             85.4%;  Score 35;  DB 9;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 7.1e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 3
US-10-235-483-64
; Sequence 64, Application US/10235483
; Publication No. US20030087407A1
;   GENERAL INFORMATION:
;        APPLICANT: SOTO-JARA, Claudio
;                   BAUMANN, Marc
;                   FRANGIONE, Blas
;        TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                            COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                            ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                            DEPOSITS
;        NUMBER OF SEQUENCES: 69
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: BROWDY AND NEIMARK
;             STREET: 419 Seventh Street, N.W., Suite 400
;             CITY: Washington
;             STATE: D.C.
;             COUNTRY: USA
;             ZIP: 20004
;        COMPUTER READABLE FORM:
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;              MEDIUM TYPE: Floppy disk
;              COMPUTER: IBM PC compatible
;              OPERATING SYSTEM: PC-DOS/MS-DOS
;              SOFTWARE: PatentIn Release #1.0, Version #1.30
;         CURRENT APPLICATION DATA:
;              APPLICATION NUMBER: US/10/235,483
;              FILING DATE: 06-Sep-2002
;              CLASSIFICATION: <Unknown>
;         PRIOR APPLICATION DATA:
;              APPLICATION NUMBER: US/08/766,596
;              FILING DATE: <Unknown>
;              APPLICATION NUMBER: US 08/630,645
;              FILING DATE: 10-APR-1996
;              APPLICATION NUMBER: US 08/478,326
;              FILING DATE: 06-JUN-1995
;         ATTORNEY/AGENT INFORMATION:
;              NAME: YUN, Allen C.
;              REGISTRATION NUMBER: 37,971
;              REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;         TELECOMMUNICATION INFORMATION:
;              TELEPHONE: 202-628-5197
;              TELEFAX: 202-737-3528
;    INFORMATION FOR SEQ ID NO: 64:
;         SEQUENCE CHARACTERISTICS:
;              LENGTH: 9 amino acids
;              TYPE: amino acid
;              STRANDEDNESS: single
;              TOPOLOGY: linear
;         MOLECULE TYPE: peptide
;         SEQUENCE DESCRIPTION: SEQ ID NO: 64:
US-10-235-483-64

  Query Match             85.4%;  Score 35;  DB 14;  Length 9;
  Best Local Similarity   100.0%;  Pred. No. 7.1e+05;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 4
US-09-988-842-9
; Sequence 9, Application US/09988842
; Patent No. US20020143105A1
; GENERAL INFORMATION:
;  APPLICANT: Johansson, Jan
;  TITLE OF INVENTION: DISCORDANT HELIX STABILIZATION FOR PREVENTION
;  TITLE OF INVENTION:  OF AMYLOID FORMATION
;  FILE REFERENCE: 12125-002001
;  CURRENT APPLICATION NUMBER: US/09/988,842
;  CURRENT FILING DATE:  2001-11-19
;  PRIOR APPLICATION NUMBER: US 60/251,662
;  PRIOR FILING DATE: 2000-12-06
;  PRIOR APPLICATION NUMBER: US 60/253,695
;  PRIOR FILING DATE: 2000-11-20
;  NUMBER OF SEQ ID NOS: 26
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;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 9
;   LENGTH: 11
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetically generated peptide
US-09-988-842-9

  Query Match             85.4%;  Score 35;  DB 9;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 1.4;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 5
US-09-988-842-25
; Sequence 25, Application US/09988842
; Patent No. US20020143105A1
; GENERAL INFORMATION:
;  APPLICANT: Johansson, Jan
;  TITLE OF INVENTION: DISCORDANT HELIX STABILIZATION FOR PREVENTION
;  TITLE OF INVENTION:  OF AMYLOID FORMATION
;  FILE REFERENCE: 12125-002001
;  CURRENT APPLICATION NUMBER: US/09/988,842
;  CURRENT FILING DATE:  2001-11-19
;  PRIOR APPLICATION NUMBER: US 60/251,662
;  PRIOR FILING DATE: 2000-12-06
;  PRIOR APPLICATION NUMBER: US 60/253,695
;  PRIOR FILING DATE: 2000-11-20
;  NUMBER OF SEQ ID NOS: 26
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 25
;   LENGTH: 11
;   TYPE: PRT
;   ORGANISM: Artificial Sequence
;   FEATURE:
;   OTHER INFORMATION: Synthetically generated peptide
US-09-988-842-25

  Query Match             85.4%;  Score 35;  DB 9;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 1.4;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9


RESULT 6
US-10-235-483-14
; Sequence 14, Application US/10235483
; Publication No. US20030087407A1
;   GENERAL INFORMATION:
```

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;         APPLICANT: SOTO-JARA, Claudio
;                    BAUMANN, Marc
;                    FRANGIONE, Blas
;         TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                             COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                             ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                             DEPOSITS
;         NUMBER OF SEQUENCES: 69
;         CORRESPONDENCE ADDRESS:
;              ADDRESSEE: BROWDY AND NEIMARK
;              STREET: 419 Seventh Street, N.W., Suite 400
;              CITY: Washington
;              STATE: D.C.
;              COUNTRY: USA
;              ZIP: 20004
;         COMPUTER READABLE FORM:
;              MEDIUM TYPE: Floppy disk
;              COMPUTER: IBM PC compatible
;              OPERATING SYSTEM: PC-DOS/MS-DOS
;              SOFTWARE: PatentIn Release #1.0, Version #1.30
;         CURRENT APPLICATION DATA:
;              APPLICATION NUMBER: US/10/235,483
;              FILING DATE: 06-Sep-2002
;              CLASSIFICATION: <Unknown>
;         PRIOR APPLICATION DATA:
;              APPLICATION NUMBER: US/08/766,596
;              FILING DATE: <Unknown>
;              APPLICATION NUMBER: US 08/630,645
;              FILING DATE: 10-APR-1996
;              APPLICATION NUMBER: US 08/478,326
;              FILING DATE: 06-JUN-1995
;         ATTORNEY/AGENT INFORMATION:
;              NAME: YUN, Allen C.
;              REGISTRATION NUMBER: 37,971
;              REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;         TELECOMMUNICATION INFORMATION:
;              TELEPHONE: 202-628-5197
;              TELEFAX: 202-737-3528
;    INFORMATION FOR SEQ ID NO: 14:
;         SEQUENCE CHARACTERISTICS:
;              LENGTH: 11 amino acids
;              TYPE: amino acid
;              STRANDEDNESS: single
;              TOPOLOGY: linear
;         MOLECULE TYPE: peptide
;         SEQUENCE DESCRIPTION: SEQ ID NO: 14:
US-10-235-483-14

  Query Match             85.4%;  Score 35;  DB 14;  Length 11;
  Best Local Similarity   100.0%;  Pred. No. 1.4;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          3 LVFFAED 9
```

```
RESULT 7
US-10-281-458-1
; Sequence 1, Application US/10281458
; Publication No. US20030108978A1
; GENERAL INFORMATION:
;  APPLICANT: Ciambrone, Gary J.
;  APPLICANT:  Gibbons, Ian
;  TITLE OF INVENTION: Whole Cell Assay Systems for Cell
;  TITLE OF INVENTION:  Surface Proteases
;  FILE REFERENCE: 50225-8093.US03
;  CURRENT APPLICATION NUMBER: US/10/281,458
;  CURRENT FILING DATE:  2002-10-25
;  PRIOR APPLICATION NUMBER: US 60/337,641
;  PRIOR FILING DATE: 2001-10-25
;  PRIOR APPLICATION NUMBER: US 09/924,692
;  PRIOR FILING DATE: 2001-08-08
;  NUMBER OF SEQ ID NOS: 3
;  SOFTWARE: FastSEQ for Windows Version 4.0
; SEQ ID NO 1
;   LENGTH: 13
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-281-458-1

  Query Match             85.4%;  Score 35;  DB 14;  Length 13;
  Best Local Similarity   100.0%;  Pred. No. 1.7;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          7 LVFFAED 13


RESULT 8
US-09-992-800-5
; Sequence 5, Application US/09992800
; Patent No. US20020102261A1
; GENERAL INFORMATION:
;  APPLICANT: Raso, Victor
;  TITLE OF INVENTION: IMMUNOLOGICAL CONTROL OF BETA-AMYLOID LEVELS IN VIVO
;  FILE REFERENCE: BBRI-2006
;  CURRENT APPLICATION NUMBER: US/09/992,800
;  CURRENT FILING DATE:  2001-11-06
;  PRIOR APPLICATION NUMBER: 09/594,366
;  PRIOR FILING DATE: 2000-06-15
;  PRIOR APPLICATION NUMBER: 60/139,408
;  PRIOR FILING DATE: 1999-06-16
;  NUMBER OF SEQ ID NOS: 7
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 5
;   LENGTH: 14
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-992-800-5
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  Query Match             85.4%;  Score 35;  DB 9;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 1.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          5 LVFFAED 11


RESULT 9
US-09-992-994-5
; Sequence 5, Application US/09992994
; Patent No. US20020136718A1
; GENERAL INFORMATION:
;  APPLICANT: Raso, Victor
;  TITLE OF INVENTION: IMMUNOLOGICAL CONTROL OF BETA-AMYLOID LEVELS IN VIVO
;  FILE REFERENCE: BBRI-2005
;  CURRENT APPLICATION NUMBER: US/09/992,994
;  CURRENT FILING DATE:  2001-11-06
;  PRIOR APPLICATION NUMBER: 09/594,366
;  PRIOR FILING DATE: 2000-06-15
;  PRIOR APPLICATION NUMBER: 60/139,408
;  PRIOR FILING DATE: 1999-06-16
;  NUMBER OF SEQ ID NOS: 7
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 5
;   LENGTH: 14
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-992-994-5

  Query Match             85.4%;  Score 35;  DB 9;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 1.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          5 LVFFAED 11


RESULT 10
US-10-385-065-5
; Sequence 5, Application US/10385065
; Publication No. US20030235897A1
; GENERAL INFORMATION:
;  APPLICANT: Raso, Victor
;  TITLE OF INVENTION: IMMUNOLOGICAL CONTROL OF BETA-AMYLOID LEVELS IN VIVO
;  FILE REFERENCE: BBRI-2004
;  CURRENT APPLICATION NUMBER: US/10/385,065
;  CURRENT FILING DATE:  2003-03-10
;  PRIOR APPLICATION NUMBER: US/09/594,366
;  PRIOR FILING DATE: 2000-06-15
;  PRIOR APPLICATION NUMBER: 60/139,408
;  PRIOR FILING DATE: 1999-06-16
;  NUMBER OF SEQ ID NOS: 7
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 5
```

```
;   LENGTH: 14
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-10-385-065-5

  Query Match             85.4%;  Score 35;  DB 15;  Length 14;
  Best Local Similarity   100.0%;  Pred. No. 1.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          5 LVFFAED 11


RESULT 11
US-09-972-475-14
; Sequence 14, Application US/09972475
; Patent No. US20020098173A1
;   GENERAL INFORMATION:
;        APPLICANT: Findeis, Mark A. et al.
;        TITLE OF INVENTION: Modulators of Amyloid Aggregation
;        NUMBER OF SEQUENCES: 45
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: LAHIVE & COCKFIELD, LLP
;             STREET: 28 State Street
;             CITY: Boston
;             STATE: Massachusetts
;             COUNTRY: USA
;             ZIP: 02109-1875
;        COMPUTER READABLE FORM:
;             MEDIUM TYPE: Floppy disk
;             COMPUTER: IBM PC compatible
;             OPERATING SYSTEM: PC-DOS/MS-DOS
;             SOFTWARE: PatentIn Release #1.0, Version #1.25
;        CURRENT APPLICATION DATA:
;             APPLICATION NUMBER: US/09/972,475
;             FILING DATE: 04-Oct-2001
;        PRIOR APPLICATION DATA:
;             APPLICATION NUMBER: 08/617,267
;             FILING DATE: <Unknown>
;             APPLICATION NUMBER: USSN 08/475,579
;             FILING DATE: 07-JUN-1995
;             APPLICATION NUMBER: USSN 08/548,998
;             FILING DATE: 27-OCT-1995
;        ATTORNEY/AGENT INFORMATION:
;             NAME: DeConti, Giulio A.
;             REGISTRATION NUMBER: 31,503
;             REFERENCE/DOCKET NUMBER: PPI-002CP2
;        TELECOMMUNICATION INFORMATION:
;             TELEPHONE: (617)227-7400
;             TELEFAX: (617)227-5941
;   INFORMATION FOR SEQ ID NO: 14:
;        SEQUENCE CHARACTERISTICS:
;             LENGTH: 15 amino acids
;             TYPE: amino acid
;             TOPOLOGY: linear
;        MOLECULE TYPE: peptide
```

```
;         FRAGMENT TYPE: internal
;         SEQUENCE DESCRIPTION: SEQ ID NO: 14:
US-09-972-475-14

  Query Match             85.4%;  Score 35;  DB 9;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 1.9;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 12
US-09-996-357-9
; Sequence 9, Application US/09996357
; Patent No. US20020133001A1
; GENERAL INFORMATION:
;  APPLICANT: Gefter, Malcolm L
;  APPLICANT:  Isreal, David I
;  APPLICANT:  Joyal, John L
;  APPLICANT:  Gosselin, Michael
;  TITLE OF INVENTION: THERAPEUTIC AGENTS AND METHODS OF USE THEREOF FOR
;  TITLE OF INVENTION:  TREATING AN AMYLOIDOGENIC DISEASE
;  FILE REFERENCE: PPI-105
;  CURRENT APPLICATION NUMBER: US/09/996,357
;  CURRENT FILING DATE:  2001-11-27
;  PRIOR APPLICATION NUMBER: 60/253,302
;  PRIOR FILING DATE: 2000-11-27
;  PRIOR APPLICATION NUMBER: 60/250,198
;  PRIOR FILING DATE: 2000-11-29
;  PRIOR APPLICATION NUMBER: 60/257,186
;  PRIOR FILING DATE: 2000-12-20
;  NUMBER OF SEQ ID NOS: 13
;  SOFTWARE: PatentIn Ver. 2.0
; SEQ ID NO 9
;   LENGTH: 15
;   TYPE: PRT
;   ORGANISM: Homo sapiens
US-09-996-357-9

  Query Match             85.4%;  Score 35;  DB 9;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 1.9;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          2 LVFFAED 8


RESULT 13
US-10-235-483-56
; Sequence 56, Application US/10235483
; Publication No. US20030087407A1
;   GENERAL INFORMATION:
;        APPLICANT: SOTO-JARA, Claudio
;                   BAUMANN, Marc
```

```
;                    FRANGIONE, Blas
;         TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                             COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                             ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                             DEPOSITS
;         NUMBER OF SEQUENCES: 69
;         CORRESPONDENCE ADDRESS:
;              ADDRESSEE: BROWDY AND NEIMARK
;              STREET: 419 Seventh Street, N.W., Suite 400
;              CITY: Washington
;              STATE: D.C.
;              COUNTRY: USA
;              ZIP: 20004
;         COMPUTER READABLE FORM:
;              MEDIUM TYPE: Floppy disk
;              COMPUTER: IBM PC compatible
;              OPERATING SYSTEM: PC-DOS/MS-DOS
;              SOFTWARE: PatentIn Release #1.0, Version #1.30
;         CURRENT APPLICATION DATA:
;              APPLICATION NUMBER: US/10/235,483
;              FILING DATE: 06-Sep-2002
;              CLASSIFICATION: <Unknown>
;         PRIOR APPLICATION DATA:
;              APPLICATION NUMBER: US/08/766,596
;              FILING DATE: <Unknown>
;              APPLICATION NUMBER: US 08/630,645
;              FILING DATE: 10-APR-1996
;              APPLICATION NUMBER: US 08/478,326
;              FILING DATE: 06-JUN-1995
;         ATTORNEY/AGENT INFORMATION:
;              NAME: YUN, Allen C.
;              REGISTRATION NUMBER: 37,971
;              REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;         TELECOMMUNICATION INFORMATION:
;              TELEPHONE: 202-628-5197
;              TELEFAX: 202-737-3528
;    INFORMATION FOR SEQ ID NO: 56:
;         SEQUENCE CHARACTERISTICS:
;              LENGTH: 15 amino acids
;              TYPE: amino acid
;              STRANDEDNESS: single
;              TOPOLOGY: linear
;         MOLECULE TYPE: peptide
;         SEQUENCE DESCRIPTION: SEQ ID NO: 56:
US-10-235-483-56

  Query Match             85.4%;  Score 35;  DB 14;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 1.9;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          6 LVFFAED 12
```

```
RESULT 14
US-10-235-483-57
; Sequence 57, Application US/10235483
; Publication No. US20030087407A1
;   GENERAL INFORMATION:
;        APPLICANT: SOTO-JARA, Claudio
;                   BAUMANN, Marc
;                   FRANGIONE, Blas
;        TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                            COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                            ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                            DEPOSITS
;        NUMBER OF SEQUENCES: 69
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: BROWDY AND NEIMARK
;             STREET: 419 Seventh Street, N.W., Suite 400
;             CITY: Washington
;             STATE: D.C.
;             COUNTRY: USA
;             ZIP: 20004
;        COMPUTER READABLE FORM:
;             MEDIUM TYPE: Floppy disk
;             COMPUTER: IBM PC compatible
;             OPERATING SYSTEM: PC-DOS/MS-DOS
;             SOFTWARE: PatentIn Release #1.0, Version #1.30
;        CURRENT APPLICATION DATA:
;             APPLICATION NUMBER: US/10/235,483
;             FILING DATE: 06-Sep-2002
;             CLASSIFICATION: <Unknown>
;        PRIOR APPLICATION DATA:
;             APPLICATION NUMBER: US/08/766,596
;             FILING DATE: <Unknown>
;             APPLICATION NUMBER: US 08/630,645
;             FILING DATE: 10-APR-1996
;             APPLICATION NUMBER: US 08/478,326
;             FILING DATE: 06-JUN-1995
;        ATTORNEY/AGENT INFORMATION:
;             NAME: YUN, Allen C.
;             REGISTRATION NUMBER: 37,971
;             REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;        TELECOMMUNICATION INFORMATION:
;             TELEPHONE: 202-628-5197
;             TELEFAX: 202-737-3528
;   INFORMATION FOR SEQ ID NO: 57:
;        SEQUENCE CHARACTERISTICS:
;             LENGTH: 15 amino acids
;             TYPE: amino acid
;             STRANDEDNESS: single
;             TOPOLOGY: linear
;        MOLECULE TYPE: peptide
;        SEQUENCE DESCRIPTION: SEQ ID NO: 57:
US-10-235-483-57

  Query Match             85.4%;  Score 35;  DB 14;  Length 15;
  Best Local Similarity   100.0%;  Pred. No. 1.9;
```

```
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db          6 LVFFAED 12


RESULT 15
US-10-235-483-58
; Sequence 58, Application US/10235483
; Publication No. US20030087407A1
;   GENERAL INFORMATION:
;        APPLICANT: SOTO-JARA, Claudio
;                   BAUMANN, Marc
;                   FRANGIONE, Blas
;        TITLE OF INVENTION: PEPTIDES AND PHARMACEUTICAL
;                            COMPOSITIONS THEREOF FOR TREATMENT OF DISORDERS OR
DISEASES
;                            ASSOCIATED WITH PROTEIN FOLDING INTO AMYLOID OR
AMYLOID-LIKE
;                            DEPOSITS
;        NUMBER OF SEQUENCES: 69
;        CORRESPONDENCE ADDRESS:
;             ADDRESSEE: BROWDY AND NEIMARK
;             STREET: 419 Seventh Street, N.W., Suite 400
;             CITY: Washington
;             STATE: D.C.
;             COUNTRY: USA
;             ZIP: 20004
;        COMPUTER READABLE FORM:
;             MEDIUM TYPE: Floppy disk
;             COMPUTER: IBM PC compatible
;             OPERATING SYSTEM: PC-DOS/MS-DOS
;             SOFTWARE: PatentIn Release #1.0, Version #1.30
;        CURRENT APPLICATION DATA:
;             APPLICATION NUMBER: US/10/235,483
;             FILING DATE: 06-Sep-2002
;             CLASSIFICATION: <Unknown>
;        PRIOR APPLICATION DATA:
;             APPLICATION NUMBER: US/08/766,596
;             FILING DATE: <Unknown>
;             APPLICATION NUMBER: US 08/630,645
;             FILING DATE: 10-APR-1996
;             APPLICATION NUMBER: US 08/478,326
;             FILING DATE: 06-JUN-1995
;        ATTORNEY/AGENT INFORMATION:
;             NAME: YUN, Allen C.
;             REGISTRATION NUMBER: 37,971
;             REFERENCE/DOCKET NUMBER: SOTO-JARA=1A
;        TELECOMMUNICATION INFORMATION:
;             TELEPHONE: 202-628-5197
;             TELEFAX: 202-737-3528
;   INFORMATION FOR SEQ ID NO: 58:
;        SEQUENCE CHARACTERISTICS:
;             LENGTH: 15 amino acids
;             TYPE: amino acid
;             STRANDEDNESS: single
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; TOPOLOGY: linear
; MOLECULE TYPE: peptide
; SEQUENCE DESCRIPTION: SEQ ID NO: 58:
US-10-235-483-58

Query Match 85.4%; Score 35; DB 14; Length 15;
Best Local Similarity 100.0%; Pred. No. 1.9;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy          1 LVFFAED 7
              |||||||
Db          6 LVFFAED 12
```

Search completed: March 4, 2004, 15:57:37
Job time : 0.893617 secs

GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 4, 2004, 15:28:35 ; Search time 1.14894 Seconds
(without alignments)
2196.942 Million cell updates/sec

Title: US-09-668-314C-84
Perfect score: 41
Sequence: 1 LVFFAEDF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 1017041 seqs, 315518202 residues

Total number of hits satisfying chosen parameters: 1017041

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SPTREMBL_25:*
1: sp_archea:*
2: sp_bacteria:*
3: sp_fungi:*
4: sp_human:*
5: sp_invertebrate:*
6: sp_mammal:*
7: sp_mhc:*
8: sp_organelle:*
9: sp_phage:*
10: sp_plant:*
11: sp_rodent:*
12: sp_virus:*
13: sp_vertebrate:*
14: sp_unclassified:*
15: sp_rvirus:*
16: sp_bacteriap:*
17: sp_archeap:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description

1	35	85.4	28	4	Q9UCD1	Q9ucd1 homo sapien
2	35	85.4	30	4	Q9UCA9	Q9uca9 homo sapien
3	35	85.4	33	4	Q9UC33	Q9uc33 homo sapien
4	35	85.4	79	11	O35463	O35463 cricetulus
5	35	85.4	82	4	Q16020	Q16020 homo sapien
6	35	85.4	82	4	Q16014	Q16014 homo sapien
7	35	85.4	82	4	Q16019	Q16019 homo sapien
8	35	85.4	113	13	Q8JH58	Q8jh58 chelydra se
9	35	85.4	218	11	Q8BPV5	Q8bpv5 mus musculu
10	35	85.4	295	16	Q8E547	Q8e547 streptococc
11	35	85.4	295	16	Q8DZI3	Q8dzi3 streptococc
12	35	85.4	357	13	Q8UUI8	Q8uui8 brachydanio
13	35	85.4	361	8	O20025	O20025 crithmum ma
14	35	85.4	361	8	O20011	O20011 anthriscus
15	35	85.4	364	8	O20068	O20068 neogoezia m
16	35	85.4	384	11	Q8BPC7	Q8bpc7 mus musculu
17	35	85.4	472	13	Q8UUS0	Q8uus0 brachydanio
18	35	85.4	534	13	O93296	O93296 gallus gall
19	35	85.4	569	13	Q9PVL1	Q9pvl1 gallus gall
20	35	85.4	612	13	Q9I9E7	Q9i9e7 brachydanio
21	35	85.4	678	13	Q7ZZT1	Q7zzt1 brachydanio
22	35	85.4	695	13	Q9DGJ8	Q9dgj8 gallus gall
23	35	85.4	738	13	Q90W28	Q90w28 brachydanio
24	35	85.4	751	13	Q9DGJ7	Q9dgj7 gallus gall
25	35	85.4	1169	5	Q8T9D3	Q8t9d3 drosophila
26	35	85.4	1169	5	Q9VSJ6	Q9vsj6 drosophila
27	33	80.5	222	5	Q21915	Q21915 caenorhabdi
28	33	80.5	261	6	Q9XSI7	Q9xsi7 bos taurus
29	33	80.5	448	16	Q87M09	Q87m09 vibrio para
30	33	80.5	455	17	Q50563	Q50563 methanobact
31	33	80.5	502	5	O62511	O62511 caenorhabdi
32	33	80.5	651	17	Q8THF4	Q8thf4 methanosarc
33	33	80.5	3610	5	Q968T7	Q968t7 plasmodium
34	33	80.5	3620	5	Q968T6	Q968t6 plasmodium
35	33	80.5	3628	5	Q968Y0	Q968y0 plasmodium
36	33	80.5	3704	5	Q8IKY8	Q8iky8 plasmodium
37	32	78.0	60	5	Q9BHZ8	Q9bhz8 globodera r
38	32	78.0	75	12	Q90160	Q90160 bombyx mori
39	32	78.0	184	16	Q931V3	Q931v3 staphylococ
40	32	78.0	261	2	Q7X225	Q7x225 staphylococ
41	32	78.0	261	2	Q7WRM0	Q7wrm0 staphylococ
42	32	78.0	261	16	Q99V89	Q99v89 staphylococ
43	32	78.0	268	16	Q8NXD0	Q8nxd0 staphylococ
44	32	78.0	379	16	Q83NF3	Q83nf3 tropheryma
45	32	78.0	390	16	Q83N16	Q83n16 tropheryma

ALIGNMENTS

RESULT 1
Q9UCD1
ID   Q9UCD1   PRELIMINARY;   PRT;   28 AA.
AC   Q9UCD1;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)

```
DE   Beta-amyloid peptide (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE.
RX   MEDLINE=94045685; PubMed=8229004;
RA   Vigo-Pelfrey C., Lee D., Keim P., Lieberburg I., Schenk D.B.;
RT   "Characterization of beta-amyloid peptide from human cerebrospinal
RT   fluid.";
RL   J. Neurochem. 61:1965-1968(1993).
DR   HSSP; P05067; 1AMB.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
SQ   SEQUENCE   28 AA;  3244 MW;  DE7BD081160AFC81 CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 28;
  Best Local Similarity   100.0%;  Pred. No. 3.4;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         17 LVFFAED 23


RESULT 2
Q9UCA9
ID   Q9UCA9      PRELIMINARY;      PRT;    30 AA.
AC   Q9UCA9;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Beta-amyloid protein (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE.
RX   MEDLINE=94153015; PubMed=8109908;
RA   Wisniewski T., Lalowski M., Levy E., Marques M.R., Frangione B.;
RT   "The amino acid sequence of neuritic plaque amyloid from a familial
RT   Alzheimer's disease patient.";
RL   Ann. Neurol. 35:245-246(1994).
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
SQ   SEQUENCE   30 AA;  3391 MW;  FF4167ABD081160A CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 30;
  Best Local Similarity   100.0%;  Pred. No. 3.7;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
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                 |||||||
Db          17 LVFFAED 23


RESULT 3
Q9UC33
ID   Q9UC33      PRELIMINARY;      PRT;    33 AA.
AC   Q9UC33;
DT   01-MAY-2000 (TrEMBLrel. 13, Created)
DT   01-MAY-2000 (TrEMBLrel. 13, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE.
RX   MEDLINE=93024877; PubMed=1406936;
RA   Seubert P., Vigo-Pelfrey C., Esch F., Lee M., Dovey H., Davis D.,
RA   Sinha S., Schlossmacher M., Whaley J., Swindlehurst C.;
RT   "Isolation and quantification of soluble Alzheimer's beta-peptide from
RT   biological fluids.";
RL   Nature 359:325-327(1992).
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
SQ   SEQUENCE   33 AA;  3674 MW;  B1DEFE2F4167ABD0 CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 33;
  Best Local Similarity   100.0%;  Pred. No. 4;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy           1 LVFFAED 7
                 |||||||
Db          17 LVFFAED 23


RESULT 4
O35463
ID   O35463      PRELIMINARY;      PRT;    79 AA.
AC   O35463;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Alzheimer's amyloid beta protein (Fragment).
GN   BETA APP.
OS   Cricetulus griseus (Chinese hamster).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Cricetinae;
OC   Cricetulus.
OX   NCBI_TaxID=10029;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Sambamurti K., Pinnix I., Gandhi S.;
RL   Submitted (OCT-1997) to the EMBL/GenBank/DDBJ databases.
```

```
DR   EMBL; AF030413; AAB86608.1; -.
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      79     79
SQ   SEQUENCE   79 AA;  8538 MW;  37F2C6C3BFF3F597 CRC64;

  Query Match             85.4%;  Score 35;  DB 11;  Length 79;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         37 LVFFAED 43


RESULT 5
Q16020
ID   Q16020      PRELIMINARY;      PRT;    82 AA.
AC   Q16020;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61383; AAB26265.2; -.
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8882 MW;  F534AA5AE5D9230A CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         34 LVFFAED 40


RESULT 6
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```
Q16014
ID   Q16014      PRELIMINARY;      PRT;    82 AA.
AC   Q16014;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S60721; AAB26263.2; -.
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8972 MW;  F534AA5B3EA9230A CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         34 LVFFAED 40


RESULT 7
Q16019
ID   Q16019      PRELIMINARY;      PRT;    82 AA.
AC   Q16019;
DT   01-NOV-1996 (TrEMBLrel. 01, Created)
DT   01-NOV-1996 (TrEMBLrel. 01, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Beta-amyloid peptide (Fragment).
GN   BETA APP.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=93236601; PubMed=8476439;
RA   Denman R.B., Rosenzcwaig R., Miller D.L.;
RT   "A system for studying the effect(s) of familial Alzheimer disease
RT   mutations on the processing of the beta-amyloid peptide precursor.";
RL   Biochem. Biophys. Res. Commun. 192:96-103(1993).
DR   EMBL; S61380; AAB26264.2; -.
```

```
DR   HSSP; P05067; 1BA4.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
FT   NON_TER       1      1
FT   NON_TER      82     82
SQ   SEQUENCE   82 AA;  8938 MW;  F534AA50E579230A CRC64;

  Query Match             85.4%;  Score 35;  DB 4;  Length 82;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         34 LVFFAED 40


RESULT 8
Q8JH58
ID   Q8JH58      PRELIMINARY;      PRT;   113 AA.
AC   Q8JH58;
DT   01-OCT-2002 (TrEMBLrel. 22, Created)
DT   01-OCT-2002 (TrEMBLrel. 22, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Amyloid beta protein (Fragment).
OS   Chelydra serpentina serpentina (common snapping turtle).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Testudines; Cryptodira; Testudinoidea; Chelydridae; Chelydra.
OX   NCBI_TaxID=134619;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=21876906; PubMed=11882478;
RA   Trudeau V.L., Chiu S., Kennedy S.W., Brooks R.J.;
RT   "Octylphenol (OP) alters the expression of members of the amyloid
RT   protein family in the hypothalamus of the snapping turtle, Chelydra
RT   serpentina serpentina.";
RL   Environ. Health Perspect. 110:269-275(2002).
DR   EMBL; AF541917; AAN04908.1; -.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   113 AA;  12750 MW;  72515C930496E053 CRC64;

  Query Match             85.4%;  Score 35;  DB 13;  Length 113;
  Best Local Similarity   100.0%;  Pred. No. 14;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         31 LVFFAED 37


RESULT 9
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```
Q8BPV5
ID   Q8BPV5      PRELIMINARY;      PRT;   218 AA.
AC   Q8BPV5;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE   Amyloid beta (Fragment).
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=C57BL/6J; TISSUE=Lung;
RX   MEDLINE=22354683; PubMed=12466851;
RA   The FANTOM Consortium,
RA   the RIKEN Genome Exploration Research Group Phase I & II Team;
RT   "Analysis of the mouse transcriptome based on functional annotation of
RT   60,770 full-length cDNAs.";
RL   Nature 420:563-573(2002).
DR   EMBL; AK052448; BAC34997.1; -.
DR   MGD; MGI:88059; App.
DR   GO; GO:0005515; F:protein binding; IPI.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   218 AA;  24118 MW;  95B55AFDAE1D0EF5 CRC64;

  Query Match             85.4%;  Score 35;  DB 11;  Length 218;
  Best Local Similarity   100.0%;  Pred. No. 28;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        136 LVFFAED 142


RESULT 10
Q8E547
ID   Q8E547      PRELIMINARY;      PRT;   295 AA.
AC   Q8E547;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE   Hypothetical protein.
GN   GBS1185.
OS   Streptococcus agalactiae (serotype III).
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=216495;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=NEM316 / Serotype III;
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RX   MEDLINE=22242508; PubMed=12354221;
RA   Glaser P., Rusniok C., Buchrieser C., Chevalier F., Frangeul L.,
RA   Msadek T., Zouine M., Couve E., Lalioui L., Poyart C., Trieu-Cuot P.,
RA   Kunst F.;
RT   "Genome sequence of Streptococcus agalactiae, a pathogen causing
RT   invasive neonatal disease.";
RL   Mol. Microbiol. 45:1499-1513(2002).
DR   EMBL; AL766849; CAD46844.1; -.
DR   SagaList; gbs1185; -.
DR   GO; GO:0005576; C:extracellular; IEA.
DR   GO; GO:0016020; C:membrane; IEA.
DR   GO; GO:0005179; F:hormone activity; IEA.
DR   InterPro; IPR000187; corticoliberin.
DR   InterPro; IPR000620; DUF6.
DR   InterPro; IPR004626; RarD.
DR   Pfam; PF00892; DUF6; 1.
DR   TIGRFAMs; TIGR00688; rarD; 1.
DR   PROSITE; PS00511; CRF; 1.
KW   Hypothetical protein; Complete proteome.
SQ   SEQUENCE   295 AA;  33015 MW;  60DDE324099DD314 CRC64;

  Query Match             85.4%;  Score 35;  DB 16;  Length 295;
  Best Local Similarity   75.0%;  Pred. No. 38;
  Matches    6;  Conservative    2;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAEDF 8
              :|||||:||
Db        196 IVFFAKDF 203


RESULT 11
Q8DZI3
ID   Q8DZI3      PRELIMINARY;      PRT;   295 AA.
AC   Q8DZI3;
DT   01-MAR-2003 (TrEMBLrel. 23, Created)
DT   01-MAR-2003 (TrEMBLrel. 23, Last sequence update)
DT   01-OCT-2003 (TrEMBLrel. 25, Last annotation update)
DE   RarD protein.
GN   RARD OR SAG1118.
OS   Streptococcus agalactiae (serotype V).
OC   Bacteria; Firmicutes; Lactobacillales; Streptococcaceae;
OC   Streptococcus.
OX   NCBI_TaxID=216466;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=2603 V/R / Serotype V;
RX   MEDLINE=22222988; PubMed=12200547;
RA   Tettelin H., Masignani V., Cieslewicz M.J., Eisen J.A., Peterson S.,
RA   Wessels M.R., Paulsen I.T., Nelson K.E., Margarit I., Read T.D.,
RA   Madoff L.C., Wolf A.M., Beanan M.J., Brinkac L.M., Daugherty S.C.,
RA   DeBoy R.T., Durkin A.S., Kolonay J.F., Madupu R., Lewis M.R.,
RA   Radune D., Fedorova N.B., Scanlan D., Khouri H., Mulligan S.,
RA   Carty H.A., Cline R.T., Van Aken S.E., Gill J., Scarselli M., Mora M.,
RA   Iacobini E.T., Brettoni C., Galli G., Mariani M., Vegni F., Maione D.,
RA   Rinaudo D., Rappuoli R., Telford J.L., Kasper D.L., Grandi G.,
RA   Fraser C.M.;
RT   "Complete genome sequence and comparative genomic analysis of an
```

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RT   emerging human pathogen, serotype V Streptococcus agalactiae.";
RL   Proc. Natl. Acad. Sci. U.S.A. 99:12391-12396(2002).
DR   EMBL; AE014243; AAM99999.1; -.
DR   TIGR; SAG1118; -.
DR   GO; GO:0005576; C:extracellular; IEA.
DR   GO; GO:0016020; C:membrane; IEA.
DR   GO; GO:0005179; F:hormone activity; IEA.
DR   InterPro; IPR000187; corticoliberin.
DR   InterPro; IPR000620; DUF6.
DR   InterPro; IPR004626; RarD.
DR   Pfam; PF00892; DUF6; 1.
DR   TIGRFAMs; TIGR00688; rarD; 1.
DR   PROSITE; PS00511; CRF; 1.
KW   Complete proteome.
SQ   SEQUENCE   295 AA;  33015 MW;  60DDE324099DD314 CRC64;

  Query Match             85.4%;  Score 35;  DB 16;  Length 295;
  Best Local Similarity   75.0%;  Pred. No. 38;
  Matches    6;  Conservative    2;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAEDF 8
              :||||:||
Db        196 IVFFAKDF 203


RESULT 12
Q8UUI8
ID   Q8UUI8      PRELIMINARY;      PRT;   357 AA.
AC   Q8UUI8;
DT   01-MAR-2002 (TrEMBLrel. 20, Created)
DT   01-MAR-2002 (TrEMBLrel. 20, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Putative mebrane protein (Fragment).
GN   APPA.
OS   Brachydanio rerio (Zebrafish) (Danio rerio).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Actinopterygii; Neopterygii; Teleostei; Ostariophysi; Cypriniformes;
OC   Cyprinidae; Danio.
OX   NCBI_TaxID=7955;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Embryo;
RX   PubMed=11862463;
RA   Musa A., Lehrach H., Russo V.E.A.;
RT   "Distinct expression patterns of two zebrafish homologues of the human
RT   APP gene during embryonic development.";
RL   Dev. Genes Evol. 211:563-567(2001).
DR   EMBL; AJ315637; CAC85734.1; -.
DR   ZFIN; ZDB-GENE-000616-13; appa.
DR   GO; GO:0016020; C:membrane; IEA.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PROSITE; PS00320; A4_INTRA; 1.
FT   NON_TER       1      1
SQ   SEQUENCE   357 AA;  40962 MW;  07D99EEF6C55B2D8 CRC64;
```

```
  Query Match             85.4%;  Score 35;  DB 13;  Length 357;
  Best Local Similarity   100.0%;  Pred. No. 46;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        275 LVFFAED 281


RESULT 13
O20025
ID   O20025      PRELIMINARY;      PRT;   361 AA.
AC   O20025;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Intron maturase (Maturase K) (Fragment).
GN   MATK.
OS   Crithmum maritimum (samphire).
OG   Chloroplast.
OC   Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;
OC   Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots; asterids;
OC   campanulids; Apiales; Apiaceae; Apioideae; apioid superclade;
OC   Pyramidoptereae; Crithmum.
OX   NCBI_TaxID=40916;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Plunkett G.M., Soltis D.E., Soltis P.S.;
RT   "Evolutionary patterns in Apiaceae: inferences based on matK sequence
RT   data.";
RL   Syst. Bot. 21:477-495(1996).
CC   -!- FUNCTION: PROBABLY ASSISTS IN SPLICING CHLOROPLAST GROUP II
CC       INTRONS (BY SIMILARITY).
CC   -!- SIMILARITY: WITH CORRESPONDING ORF IN OTHER PLANT CHLOROPLASTS,
CC       AND REGIONS OF SIMILARITY TO MATURASE-LIKE POLYPEPTIDES ENCODED BY
CC       MITOCHONDRIAL INTRONS.
DR   EMBL; U58558; AAB66262.1; -.
DR   GO; GO:0009507; C:chloroplast; IEA.
DR   GO; GO:0006397; P:mRNA processing; IEA.
DR   InterPro; IPR002866; MatK_N.
DR   Pfam; PF01824; MatK_N; 1.
KW   mRNA processing; Chloroplast.
FT   NON_TER     361     361
SQ   SEQUENCE   361 AA;  42847 MW;  43A0657ED3134DEA CRC64;

  Query Match             85.4%;  Score 35;  DB 8;  Length 361;
  Best Local Similarity   75.0%;  Pred. No. 46;
  Matches    6;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 LVFFAEDF 8
              |:||| ||
Db         73 LIFFANDF 80


RESULT 14
O20011
```

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ID   O20011      PRELIMINARY;      PRT;   361 AA.
AC   O20011;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Intron maturase (Maturase K) (Fragment).
GN   MATK.
OS   Anthriscus sylvestris.
OG   Chloroplast.
OC   Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;
OC   Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots; asterids;
OC   campanulids; Apiales; Apiaceae; Apioideae; Scandiceae; Scandicinae;
OC   Anthriscus.
OX   NCBI_TaxID=48027;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Plunkett G.M., Soltis D.E., Soltis P.S.;
RT   "Evolutionary patterns in Apiaceae: inferences based on matK sequence
RT   data.";
RL   Syst. Bot. 21:477-495(1996).
CC   -!- FUNCTION: PROBABLY ASSISTS IN SPLICING CHLOROPLAST GROUP II
CC       INTRONS (BY SIMILARITY).
CC   -!- SIMILARITY: WITH CORRESPONDING ORF IN OTHER PLANT CHLOROPLASTS,
CC       AND REGIONS OF SIMILARITY TO MATURASE-LIKE POLYPEPTIDES ENCODED BY
CC       MITOCHONDRIAL INTRONS.
DR   EMBL; U58547; AAB66255.1; -.
DR   GO; GO:0009507; C:chloroplast; IEA.
DR   GO; GO:0006397; P:mRNA processing; IEA.
DR   InterPro; IPR002866; MatK_N.
DR   Pfam; PF01824; MatK_N; 1.
KW   mRNA processing; Chloroplast.
FT   NON_TER     361     361
SQ   SEQUENCE   361 AA;  43334 MW;  D1A875A9910B6F21 CRC64;

  Query Match             85.4%;  Score 35;  DB 8;  Length 361;
  Best Local Similarity   75.0%;  Pred. No. 46;
  Matches    6;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 LVFFAEDF 8
              |:||| ||
Db         73 LIFFANDF 80


RESULT 15
O20068
ID   O20068      PRELIMINARY;      PRT;   364 AA.
AC   O20068;
DT   01-JAN-1998 (TrEMBLrel. 05, Created)
DT   01-JAN-1998 (TrEMBLrel. 05, Last sequence update)
DT   01-JUN-2003 (TrEMBLrel. 24, Last annotation update)
DE   Intron maturase (Maturase K) (Fragment).
GN   MATK.
OS   Neogoezia minor.
OG   Chloroplast.
OC   Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta;
OC   Spermatophyta; Magnoliophyta; eudicotyledons; core eudicots; asterids;
OC   campanulids; Apiales; Apiaceae; Apioideae; Oenantheae; Neogoezia.
```

```
OX   NCBI_TaxID=46372;
RN   [1]
RP   SEQUENCE FROM N.A.
RA   Plunkett G.M., Soltis D.E., Soltis P.S.;
RT   "Evolutionary patterns in Apiaceae: inferences based on matK sequence
RT   data.";
RL   Syst. Bot. 21:477-495(1996).
RN   [2]
RP   SEQUENCE FROM N.A.
RA   Plunkett G.M., Soltis D.E., Soltis P.S.;
RT   "Clarification of the relationship between Apiaceae and Araliaceae
RT   based on matK and rbcL sequence data.";
RL   Am. J. Bot. 84:565-580(1997).
CC   -!- FUNCTION: PROBABLY ASSISTS IN SPLICING CHLOROPLAST GROUP II
CC       INTRONS (BY SIMILARITY).
CC   -!- SIMILARITY: WITH CORRESPONDING ORF IN OTHER PLANT CHLOROPLASTS,
CC       AND REGIONS OF SIMILARITY TO MATURASE-LIKE POLYPEPTIDES ENCODED BY
CC       MITOCHONDRIAL INTRONS.
DR   EMBL; U58570; AAB66281.1; -.
DR   GO; GO:0009507; C:chloroplast; IEA.
DR   GO; GO:0006397; P:mRNA processing; IEA.
DR   InterPro; IPR002866; MatK_N.
DR   Pfam; PF01824; MatK_N; 1.
KW   mRNA processing; Chloroplast.
FT   NON_TER     364     364
SQ   SEQUENCE   364 AA;  42939 MW;  DBABC9499ED36646 CRC64;

  Query Match             85.4%;  Score 35;  DB 8;  Length 364;
  Best Local Similarity   75.0%;  Pred. No. 47;
  Matches    6;  Conservative    1;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 LVFFAEDF 8
              |:||| ||
Db         76 LIFFANDF 83


Search completed: March  4, 2004, 15:38:55
Job time : 2.14894 secs
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GenCore version 5.1.6

OM protein - protein search, using sw model

Run on: March 4, 2004, 15:22:30 ; Search time 0.255319 Seconds
(without alignments)
1631.532 Million cell updates/sec

Title: US-09-668-314C-84
Perfect score: 41
Sequence: 1 LVFFAEDF 8

Scoring table: BLOSUM62
Gapop 10.0 , Gapext 0.5

Searched: 141681 seqs, 52070155 residues

Total number of hits satisfying chosen parameters: 141681

Minimum DB seq length: 0
Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%
Maximum Match 100%
Listing first 45 summaries

Database : SwissProt_42:*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
1	35	85.4	57	1	A4_URSMA	Q29149 ursus marit
2	35	85.4	58	1	A4_CANFA	Q28280 canis famil
3	35	85.4	58	1	A4_RABIT	Q28748 oryctolagus
4	35	85.4	58	1	A4_SHEEP	Q28757 ovis aries
5	35	85.4	59	1	A4_BOVIN	Q28053 bos taurus
6	35	85.4	751	1	A4_SAISC	Q95241 s amyloid b
7	35	85.4	770	1	A4_CAVPO	Q60495 c amyloid b
8	35	85.4	770	1	A4_HUMAN	P05067 h amyloid b
9	35	85.4	770	1	A4_MACFA	P53601 m amyloid b
10	35	85.4	770	1	A4_MOUSE	P12023 m amyloid b
11	35	85.4	770	1	A4_PIG	P79307 s amyloid b
12	35	85.4	770	1	A4_RAT	P08592 r amyloid b
13	35	85.4	780	1	A4_TETFL	O73683 tetraodon f
14	32	78.0	89	1	PE23_SHEEP	Q28550 ovis aries
15	32	78.0	737	1	A4_FUGRU	O93279 fugu rubrip
16	31	75.6	224	1	Y691_CHLTR	O84697 chlamydia t
17	31	75.6	281	1	UPK_CORST	Q9fb58 corynebacte

18	31	75.6	301	1	YWBI_BACSU	P39592 bacillus su
19	31	75.6	580	1	MM14_PIG	Q9xt90 sus scrofa
20	31	75.6	582	1	MM14_HUMAN	P50281 homo sapien
21	31	75.6	582	1	MM14_RABIT	Q95220 oryctolagus
22	31	75.6	622	1	YRT1_CAEEL	Q10044 caenorhabdi
23	31	75.6	956	1	MTN2_HUMAN	O00339 homo sapien
24	31	75.6	956	1	MTN2_MOUSE	O08746 mus musculu
25	31	75.6	1932	1	FAB1_SCHPO	O59722 schizosacch
26	31	75.6	2196	1	MOR2_SCHPO	Q9hdv6 schizosacch
27	30	73.2	224	1	Y681_CHLPN	Q9z7m3 chlamydia p
28	30	73.2	473	1	SYE_WIGBR	Q8d375 wiggleswort
29	30	73.2	529	1	YQP4_CAEEL	Q09531 caenorhabdi
30	30	73.2	570	1	GRAU_DROME	Q9u405 drosophila
31	30	73.2	641	1	LICR_BACSU	P46321 bacillus su
32	30	73.2	1006	1	BGAL_LACDE	P20043 lactobacill
33	30	73.2	1516	1	UGG2_HUMAN	Q9nyu1 homo sapien
34	30	73.2	1888	1	CA1E_CHICK	P32018 gallus gall
35	29	70.7	251	1	Y126_PYRAB	Q9v2e8 pyrococcus
36	29	70.7	310	1	NU1M_DALCH	O63623 dalbulus ch
37	29	70.7	321	1	Y189_RICPR	Q9zdx5 rickettsia
38	29	70.7	357	1	HST2_YEAST	P53686 saccharomyc
39	29	70.7	380	1	HYD2_BRAJA	P31904 bradyrhizob
40	29	70.7	383	1	O94B_DROME	Q9vcs8 drosophila
41	29	70.7	385	1	HYPD_RHILV	P40598 rhizobium l
42	29	70.7	420	1	SYH_MYCPU	Q98qm8 mycoplasma
43	29	70.7	438	1	CLN3_CANFA	Q29611 canis famil
44	29	70.7	438	1	CLN3_MOUSE	Q61124 mus musculu
45	29	70.7	526	1	CH62_CHLPN	Q9z7c9 chlamydia p

ALIGNMENTS

```
RESULT 1
A4_URSMA
ID   A4_URSMA       STANDARD;      PRT;    57 AA.
AC   Q29149;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Ursus maritimus (Polar bear) (Thalarctos maritimus).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Ursidae; Ursus.
OX   NCBI_TaxID=29073;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
```

```
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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CC   use by non-profit institutions as long as its content is in no way
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X56128; CAA39593.1; -.
DR   PIR; B60045; B60045.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   NON_TER      57     57
SQ   SEQUENCE   57 AA;  6172 MW;  84209D88EBA82DFA CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 57;
  Best Local Similarity   100.0%;  Pred. No. 0.73;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28


RESULT 2
A4_CANFA
ID   A4_CANFA       STANDARD;      PRT;    58 AA.
AC   Q28280;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Canis familiaris (Dog).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Carnivora; Fissipedia; Canidae; Canis.
OX   NCBI_TaxID=9615;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
```

```
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   ---------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X56125; CAA39590.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         7     49       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     34       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     35     58       POTENTIAL.
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6285 MW;  8469D488A2E12DFA CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.74;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         23 LVFFAED 29


RESULT 3
A4_RABIT
ID   A4_RABIT       STANDARD;      PRT;    58 AA.
AC   Q28748;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   16-OCT-2001 (Rel. 40, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Oryctolagus cuniculus (Rabbit).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Lagomorpha; Leporidae; Oryctolagus.
OX   NCBI_TaxID=9986;
RN   [1]
```

```
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; X56129; CAA39594.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   DOMAIN       58    >58       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6300 MW;  F434209D88EBA82D CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.74;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28


RESULT 4
A4_SHEEP
ID   A4_SHEEP       STANDARD;      PRT;    58 AA.
AC   Q28757;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
```

```
OS   Ovis aries (Sheep).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Ovis.
OX   NCBI_TaxID=9940;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Heart;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56130; CAA39595.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         6     48       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     33       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     34     57       POTENTIAL.
FT   DOMAIN       58    >58       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      58     58
SQ   SEQUENCE   58 AA;  6300 MW;  F434209D88EBA82D CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 58;
  Best Local Similarity   100.0%;  Pred. No. 0.74;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db         22 LVFFAED 28


RESULT 5
A4_BOVIN
ID   A4_BOVIN       STANDARD;      PRT;    59 AA.
AC   Q28053;
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DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   30-MAY-2000 (Rel. 39, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog [Contains: Beta-amyloid
DE   protein (Beta-APP) (A-beta)] (Fragment).
GN   APP.
OS   Bos taurus (Bovine).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Bovinae; Bos.
OX   NCBI_TaxID=9913;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X56124; CAA39589.1; -.
DR   EMBL; X56126; CAA39591.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR001255; Beta-APP.
DR   Pfam; PF03494; Beta-APP; 1.
DR   PROSITE; PS00319; A4_EXTRA; PARTIAL.
DR   PROSITE; PS00320; A4_INTRA; PARTIAL.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane.
FT   NON_TER       1      1
FT   CHAIN         7     49       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       <1     34       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     35     58       POTENTIAL.
FT   DOMAIN       59    >59       CYTOPLASMIC (POTENTIAL).
FT   NON_TER      59     59
SQ   SEQUENCE   59 AA;  6414 MW;  F43469D488A2E12D CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 59;
  Best Local Similarity   100.0%;  Pred. No. 0.76;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
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Db          23 LVFFAED 29


RESULT 6
A4_SAISC
ID   A4_SAISC       STANDARD;      PRT;   751 AA.
AC   Q95241;
DT   15-DEC-1998 (Rel. 37, Created)
DT   15-DEC-1998 (Rel. 37, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha); Soluble
DE   APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-APP42);
DE   Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40); Gamma-
DE   CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Saimiri sciureus (Common squirrel monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Platyrrhini; Cebidae; Cebinae; Saimiri.
OX   NCBI_TaxID=9521;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney, and Liver;
RX   MEDLINE=96108492; PubMed=8532114;
RA   Levy E., Amorim A., Frangione B., Walker L.C.;
RT   "Beta-amyloid precursor protein gene in squirrel monkeys with
RT   cerebral amyloid angiopathy.";
RL   Neurobiol. Aging 16:805-808(1995).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction. In vitro, copper-metallated APP induces neuronal
CC       death directly or is potentiated through Cu(II)-mediated low-
CC       density lipoprotein oxidation (By similarity). Can regulate
CC       neurite outgrowth through binding to components of the
CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
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CC       family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
CC       maturation occurs (O-glycosylated and sulfated). After alpha-
CC       secretase cleavage, soluble APP is released into the extracellular
CC       space and the C-terminal is internalized to endosomes and
CC       lysosomes. Some APP accumulates in secretory transport vesicles
CC       leaving the late Golgi compartment and returns to the cell
CC       surface. Gamma-CTF(59) peptide is located to both the cytoplasm
CC       and nuclei of neurons (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms seem to exist;
CC       Name=APP770;
CC         IsoId=Q95241-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=Q95241-2; Sequence=Not described;
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue. The NPXY site is also involved in clathrin-mediated
CC       endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       C83 and C99. Subsequent processing of C83 by gamma-secretase
CC       yields P3 peptides. This is the major secretory pathway and is
CC       nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC       gamma-secretase processing of C99 releases the amyloid beta
CC       proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC       major components of amyloid plaques, and the cytotoxic C-terminal
CC       fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
CC       similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC       (By similarity). Cleavage at Asp-720 by either caspase-3, -8 or -9
CC       results in the production of the neurotoxic C31 peptide and the
CC       increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific. Phosphorylation can affect APP
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CC       processing, neuronal differentiation and interaction with other
CC       proteins (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates (By similarity).
CC       Extracellular zinc-binding increases binding of heparin to APP and
CC       inhibits collagen-binding (By similarity).
CC   -!- SIMILARITY: Belongs to the APP family.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; S81024; AAD14347.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Amyloid; Alternative splicing.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    751       A4 PROTEIN.
FT   CHAIN        18    668       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    652       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       653    751       C99 (POTENTIAL).
FT   CHAIN       653    694       BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT   CHAIN       653    692       BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT   CHAIN       669    751       C83 (POTENTIAL).
FT   CHAIN       669    694       P3(42) (POTENTIAL).
FT   CHAIN       669    692       P3(40) (POTENTIAL).
FT   CHAIN       693    751       GAMMA-CTF(59) (POTENTIAL).
FT   CHAIN       695    751       GAMMA-CTF(57) (POTENTIAL).
FT   CHAIN       702    751       GAMMA-CTF(50) (POTENTIAL).
FT   CHAIN       721    751       C31 (POTENTIAL).
FT   DOMAIN       18    680       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    681    704       POTENTIAL.
FT   DOMAIN      705    751       CYTOPLASMIC (POTENTIAL).
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FT   DOMAIN       96    110       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      181    188       ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN      291    341       BPTI/KUNITZ INHIBITOR.
FT   DOMAIN      316    344       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      363    428       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      504    521       COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN      713    732       INTERACTION WITH G(O)-ALPHA
FT                                (BY SIMILARITY).
FT   DOMAIN      230    260       ASP/GLU-RICH (ACIDIC).
FT   DOMAIN      274    280       POLY-THR.
FT   SITE        144    144       REQUIRED FOR COPPER(II) REDUCTION
FT                                (BY SIMILARITY).
FT   ACT_SITE    301    302       REACTIVE BOND.
FT   SITE        652    653       CLEAVAGE (BY BETA-SECRETASE)
FT                                (BY SIMILARITY).
FT   SITE        653    654       CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE        668    669       CLEAVAGE (BY ALPHA-SECRETASE)
FT                                (BY SIMILARITY).
FT   SITE        685    685       INVOLVED IN FREE RADICAL PROPAGATION
FT                                (BY SIMILARITY).
FT   SITE        687    687       INVOLVED IN OXIDATIVE REACTIONS
FT                                (BY SIMILARITY).
FT   SITE        692    693       CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                (BY SIMILARITY).
FT   SITE        694    695       CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                (BY SIMILARITY).
FT   SITE        701    702       CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                                (BY SIMILARITY).
FT   SITE        705    715       BASOLATERAL SORTING SIGNAL
FT                                (BY SIMILARITY).
FT   SITE        720    721       CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)
FT                                (BY SIMILARITY).
FT   SITE        738    741       ENDOCYTOSIS SIGNAL.
FT   SITE        740    743       NPXY MOTIF.

  Query Match             85.4%;  Score 35;  DB 1;  Length 751;
  Best Local Similarity   100.0%;  Pred. No. 9.6;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        669 LVFFAED 675


RESULT 7
A4_CAVPO
ID   A4_CAVPO       STANDARD;      PRT;   770 AA.
AC   Q60495; Q60496;
DT   10-OCT-2003 (Rel. 42, Created)
DT   10-OCT-2003 (Rel. 42, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); CTF-alpha; CTF-beta; Beta-amyloid
DE   protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); P3(42);
DE   P3(40); CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-
DE   CTF(57) (Gamma-secretase C-terminal fragment 57); C31].
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GN   APP.
OS   Cavia porcellus (Guinea pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Hystricognathi; Caviidae; Cavia.
OX   NCBI_TaxID=10141;
RN   [1]
RP   SEQUENCE FROM N.A., AND ALTERNATIVE SPLICING.
RC   TISSUE=Brain, and Liver;
RX   MEDLINE=97236426; PubMed=9116031;
RA   Beck M., Mueller D., Bigl V.;
RT   "Amyloid precursor protein in Guinea pigs - complete cDNA sequence and
RT   alternative splicing.";
RL   Biochim. Biophys. Acta 1351:17-21(1997).
RN   [2]
RP   INTERACTION OF BETA-APP40 WITH APOE.
RX   MEDLINE=98007700; PubMed=9349544;
RA   Martel C.L., Mackic J.B., Matsubara E., Governale S., Miguel C.,
RA   Miao W., McComb J.G., Frangione B., Ghiso J., Zlokovic B.V.;
RT   "Isoform-specific effects of apolipoproteins E2, E3, and E4 on
RT   cerebral capillary sequestration and blood-brain barrier transport of
RT   circulating Alzheimer's amyloid beta.";
RL   J. Neurochem. 69:1995-2004(1997).
RN   [3]
RP   PROCESSING.
RX   MEDLINE=20084499; PubMed=10619481;
RA   Beck M., Brueckner M.K., Holzer M., Kaap S., Pannicke T., Arendt T.,
RA   Bigl V.;
RT   "Guinea-pig primary cell cultures provide a model to study expression
RT   and amyloidogenic processing of endogenous amyloid precursor
RT   protein.";
RL   Neuroscience 95:243-254(2000).
RN   [4]
RP   GAMMA-SECRETASE PROCESSING.
RX   MEDLINE=20576391; PubMed=11035007;
RA   Pinnix I., Musunuru U., Tun H., Sridharan A., Golde T., Eckman C.,
RA   Ziani-Cherif C., Onstead L., Sambamurti K.;
RT   "A novel gamma -secretase assay based on detection of the putative
RT   C-terminal fragment-gamma of amyloid beta protein precursor.";
RL   J. Biol. Chem. 276:481-487(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(O) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction (By similarity). In vitro, copper-metallated APP
CC       induces neuronal death directly or is potentiated through Cu(II)-
CC       mediated low-density lipoprotein oxidation (By similarity). Can
CC       regulate neurite outgrowth through binding to components of the
CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
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CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Beta-amyloid peptides bind to lipoproteins
CC       and apoliproteins E and J in the CSF and to HDL particles in
CC       plasma, inhibiting metal-catalyzed oxidation of lipoproteins.
CC   -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC       extracellular matrix and may regulate neurite outgrowth in the
CC       brain (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains), APPBP2 (via BaSS) and DDB1 (By similarity).
CC       Associates with microtubules in the presence of ATP and in a
CC       kinesin-dependent manner (By similarity). Soluble Abeta40 binds
CC       all three isoforms of APOE, in vitro and in vivo. When lipidated,
CC       ApoE3 appears to be the preferred amyloid binding isoform, while
CC       the apoE4 isoform-beta-APP40 complex is capable of being
CC       transported across the blood-brain barrier.
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated pits
CC       (By similarity). During maturation, the immature APP (N-
CC       glycosylated in the endoplasmic reticulum) moves to the Golgi
CC       complex where complete maturation occurs (O-glycosylated and
CC       sulfated) (By similarity). After alpha-secretase cleavage, soluble
CC       APP is released into the extracellular space and the C-terminal is
CC       internalized to endosomes and lysosomes (By similarity). Some APP
CC       accumulates in secretory transport vesicles leaving the late Golgi
CC       compartment and returns to the cell surface (By similarity). APP
CC       sorts to the basolateral surface in epithelial cells (By
CC       similatity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms, missing exons 7,8 and 15, seem to
CC         exist. The L-isoforms, missing exon 15, are referred to as
CC         appicans;
CC       Name=APP770;
CC         IsoId=Q60495-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=Q60495-2; Sequence=VSP_007221, VSP_007222;
CC   -!- TISSUE SPECIFICITY: Isoform APP695 is the major isoform found in
CC       brain. The longer isoforms containing the BPTI domain are
CC       predominantly expressed in peripheral organs such as muscle and
CC       liver.
CC   -!- INDUCTION: Increased levels during neuronal differentiation.
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells.
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
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CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue (By similarity). The NPXY site is also involved in
CC       clathrin-mediated endocytosis.
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       CTF-alpha and CTF-beta. Subsequent processing of CTF-alpha by
CC       gamma-secretase yields P3 peptides. This is the major secretory
CC       pathway and is nonamyloidogenic. Alternatively,
CC       presenilin/nicastrin-mediated gamma-secretase processing of CTF-
CC       beta releases the amyloid beta proteins, amyloid-beta 40 (Abeta40)
CC       and amyloid-beta 42 (Abeta42), major components of amyloid
CC       plaques, and the corresponding cytotoxic C-terminal fragments
CC       (CTFs).
CC   -!- PTM: Proteolytically cleaved by caspase-3 during neuronal
CC       apoptosis (By similarity).
CC   -!- PTM: N- and O-glycosylated. O-linkage of chondroitin sulfate to
CC       the L-APP isoforms produces the APP proteoglycan core proteins,
CC       the appicans (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific (By similarity).
CC       Phosphorylation can affect APP processing, neuronal
CC       differentiation and interaction with other proteins.
CC   -!- PTM: Extracellular binding and reduction of copper, results in a
CC       corresponding oxidation of Cys-144 and Cys-158, and the formation
CC       of a disulfide bond (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
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CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; X97631; CAA66230.1; -.
DR   EMBL; X99198; CAA67589.1; -.
DR   HSSP; P05067; 1BA4.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
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DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Alternative splicing; Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (BY SIMILARITY).
FT   CHAIN        18    671       SOLUBLE APP-BETA (BY SIMILARITY).
FT   CHAIN       672    770       CTF-ALPHA (BY SIMILARITY).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT   CHAIN       688    770       CTF-BETA (BY SIMILARITY).
FT   CHAIN       688    713       P3(42) (BY SIMILARITY).
FT   CHAIN       688    711       P3(40) (BY SIMILARITY).
FT   CHAIN       712    770       GAMMA-CTF(59) (BY SIMILARITY).
FT   CHAIN       714    770       GAMMA-CTF(57) (BY SIMILARITY).

  Query Match             85.4%;  Score 35;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694


RESULT 8
A4_HUMAN
ID   A4_HUMAN       STANDARD;      PRT;   770 AA.
AC   P05067; P09000; P78438; Q13764; Q13778; Q13793; Q16011; Q16014;
AC   Q16019; Q16020; Q9BT38; Q9UCA9; Q9UCB6; Q9UCC8; Q9UCD1; Q9UQ58;
DT   13-AUG-1987 (Rel. 05, Created)
DT   01-NOV-1991 (Rel. 20, Last sequence update)
DT   15-MAR-2004 (Rel. 43, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein) (Cerebral vascular amyloid peptide) (CVAP) (Protease
DE   nexin-II) (PN-II) (APPI) (PreA4) [Contains: Soluble APP-alpha (S-APP-
DE   alpha); Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42
DE   (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42);
DE   P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59)
DE   (Amyloid intracellular domain 59) (AID(59)); Gamma-CTF(57) (Gamma-
DE   secretase C-terminal fragment 57) (Amyloid intracellular domain 57)
DE   (AID(57)); Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50)
DE   (Amyloid intracellular domain 50) (AID(50)); C31].
GN   APP OR A4 OR AD1.
OS   Homo sapiens (Human).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
OX   NCBI_TaxID=9606;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=87144572; PubMed=2881207;
RA   Kang J., Lemaire H.-G., Unterbeck A., Salbaum J.M., Masters C.L.,
RA   Grzeschik K.-H., Multhaup G., Beyreuther K., Mueller-Hill B.;
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RT   "The precursor of Alzheimer's disease amyloid A4 protein resembles a
RT   cell-surface receptor.";
RL   Nature 325:733-736(1987).
RN   [2]
RP   SEQUENCE FROM N.A. (ISOFORM APP751).
RC   TISSUE=Brain;
RX   MEDLINE=88122639; PubMed=2893289;
RA   Ponte P., Gonzalez-Dewhitt P., Schilling J., Miller J., Hsu D.,
RA   Greenberg B., Davis K., Wallace W., Lieberburg I., Fuller F.,
RA   Cordell B.;
RT   "A new A4 amyloid mRNA contains a domain homologous to serine
RT   proteinase inhibitors.";
RL   Nature 331:525-527(1988).
RN   [3]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RX   MEDLINE=89128427; PubMed=2783775;
RA   Lemaire H.-G., Salbaum J.M., Multhaup G., Kang J., Bayney R.M.,
RA   Unterbeck A., Beyreuther K., Mueller-Hill B.;
RT   "The PreA4(695) precursor protein of Alzheimer's disease A4 amyloid
RT   is encoded by 16 exons.";
RL   Nucleic Acids Res. 17:517-522(1989).
RN   [4]
RP   SEQUENCE FROM N.A. (ISOFORM APP770).
RX   MEDLINE=90236318; PubMed=2110105;
RA   Yoshikai S.-I., Sasaki H., Doh-Ura K., Furuya H., Sakaki Y.;
RT   "Genomic organization of the human amyloid beta-protein precursor
RT   gene.";
RL   Gene 87:257-263(1990).
RN   [5]
RP   ERRATUM, AND REVISIONS.
RA   Yoshikai S.-I., Sasaki H., Doh-ura K., Furuya H., Sakaki Y.;
RL   Gene 102:291-292(1991).
RN   [6]
RP   SEQUENCE FROM N.A. (ISOFORM L-APP733).
RC   TISSUE=Leukocyte;
RX   MEDLINE=92268136; PubMed=1587857;
RA   Koenig G., Moenning U., Czech C., Prior R., Banati R.,
RA   Schreiter-Gasser U., Bauer J., Masters C.L., Beyreuther K.;
RT   "Identification and differential expression of a novel alternative
RT   splice isoform of the beta A4 amyloid precursor protein (APP) mRNA in
RT   leukocytes and brain microglial cells.";
RL   J. Biol. Chem. 267:10804-10809(1992).
RN   [7]
RP   SEQUENCE FROM N.A. (ISOFORM APP770).
RX   MEDLINE=97263807; PubMed=9108164;
RA   Hattori M., Tsukahara F., Furuhata Y., Tanahashi H., Hirose M.,
RA   Saito M., Tsukuni S., Sakaki Y.;
RT   "A novel method for making nested deletions and its application for
RT   sequencing of a 300 kb region of human APP locus.";
RL   Nucleic Acids Res. 25:1802-1808(1997).
RN   [8]
RP   SEQUENCE FROM N.A. (ISOFORM APP639).
RC   TISSUE=Brain;
RX   MEDLINE=22744650; PubMed=12859342;
RA   Tang K., Wang C., Shen C., Sheng S., Ravid R., Jing N.;
RT   "Identification of a novel alternative splicing isoform of human
RT   amyloid precursor protein gene, APP639.";
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RL Eur. J. Neurosci. 18:102-108(2003).
RN [9]
RP SEQUENCE FROM N.A. (ISOFORM APP305).
RC TISSUE=Pancreas;
RX MEDLINE=22388257; PubMed=12477932;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT "Generation and initial analysis of more than 15,000 full-length
RT human and mouse cDNA sequences.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN [10]
RP SEQUENCE OF 1-10 FROM N.A.
RC TISSUE=Liver;
RX MEDLINE=89016647; PubMed=3140222;
RA Schon E.A., Mita S., Sadlock J., Herbert J.;
RT "A cDNA specifying the human amyloid beta precursor protein (ABPP)
RT encodes a 95-kDa polypeptide.";
RL Nucleic Acids Res. 16:9351-9351(1988).
RN [11]
RP ERRATUM, AND REVISIONS.
RA Mita S., Sadlock J., Herbert J., Schon E.A.;
RL Nucleic Acids Res. 16:11402-11402(1988).
RN [12]
RP SEQUENCE OF 1-75 FROM N.A.
RX MEDLINE=89165870; PubMed=2538123;
RA La Fauci G., Lahiri D.K., Salton S.R., Robakis N.K.;
RT "Characterization of the 5'-end region and the first two exons of the
RT beta-protein precursor gene.";
RL Biochem. Biophys. Res. Commun. 159:297-304(1989).
RN [13]
RP SEQUENCE OF 18-50.
RC TISSUE=Fibroblast;
RX MEDLINE=87250462; PubMed=3597385;
RA van Nostrand W.E., Cunningham D.D.;
RT "Purification of protease nexin II from human fibroblasts.";
RL J. Biol. Chem. 262:8508-8514(1987).
RN [14]
RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP751).
RC TISSUE=Brain;
RX MEDLINE=89346754; PubMed=2569763;
RA de Sauvage F., Octave J.N.;
RT "A novel mRNA of the A4 amyloid precursor gene coding for a possibly

RT secreted protein.";
RL Science 245:651-653(1989).
RN [15]
RP PARTIAL SEQUENCE FROM N.A. (ISOFORM APP695).
RC TISSUE=Brain;
RX MEDLINE=87231971; PubMed=3035574;
RA Robakis N.K., Ramakrishna N., Wolfe G., Wisniewski H.M.;
RT "Molecular cloning and characterization of a cDNA encoding the
RT cerebrovascular and the neuritic plaque amyloid peptides.";
RL Proc. Natl. Acad. Sci. U.S.A. 84:4190-4194(1987).
RN [16]
RP SEQUENCE OF 286-366 FROM N.A.
RX MEDLINE=88122640; PubMed=2893290;
RA Tanzi R.E., McClatchey A.I., Lamperti E.D., Villa-Komaroff L.,
RA Gusella J.F., Neve R.L.;
RT "Protease inhibitor domain encoded by an amyloid protein precursor
RT mRNA associated with Alzheimer's disease.";
RL Nature 331:528-530(1988).
RN [17]
RP SEQUENCE OF 287-367 FROM N.A.
RX MEDLINE=88122641; PubMed=2893291;
RA Kitaguchi N., Takahashi Y., Tokushima Y., Shiojiri S., Ito H.;
RT "Novel precursor of Alzheimer's disease amyloid protein shows
RT protease inhibitory activity.";
RL Nature 331:530-532(1988).
RN [18]
RP SEQUENCE OF 507-770 FROM N.A.
RC TISSUE=Brain cortex;
RX MEDLINE=88124954; PubMed=2893379;
RA Zain S.B., Salim M., Chou W.G., Sajdel-Sulkowska E.M., Majocha R.E.,
RA Marotta C.A.;
RT "Molecular cloning of amyloid cDNA derived from mRNA of the Alzheimer
RT disease brain: coding and noncoding regions of the fetal precursor
RT mRNA are expressed in the cortex.";
RL Proc. Natl. Acad. Sci. U.S.A. 85:929-933(1988).
RN [19]
RP SEQUENCE OF 523-555, AND COLLAGEN-BINDING DOMAIN.
RX MEDLINE=96139497; PubMed=8576160;
RA Beher D., Hesse L., Masters C.L., Multhaup G.;
RT "Regulation of amyloid protein precursor (APP) binding to collagen and
RT mapping of the binding sites on APP and collagen type I.";
RL J. Biol. Chem. 271:1613-1620(1996).
RN [20]
RP SEQUENCE OF 655-737 FROM N.A., AND VARIANTS AD PHE-717; AD ILE-717
RP AND AD GLY-717.
RX MEDLINE=93236601; PubMed=8476439;
RA Denman R.B., Rosenzcwaig R., Miller D.L.;
RT "A system for studying the effect(s) of familial Alzheimer disease
RT mutations on the processing of the beta-amyloid peptide precursor.";
RL Biochem. Biophys. Res. Commun. 192:96-103(1993).
RN [21]
RP SEQUENCE OF 656-737 FROM N.A.
RX MEDLINE=89392030; PubMed=2675837;
RA Johnstone E.M., Chaney M.O., Moore R.E., Ward K.E., Norris F.H.,
RA Little S.P.;
RT "Alzheimer's disease amyloid peptide is encoded by two exons and shows
RT similarity to soybean trypsin inhibitor.";

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RL   Biochem. Biophys. Res. Commun. 163:1248-1255(1989).
RN   [22]

  Query Match             85.4%;  Score 35;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694


RESULT 9
A4_MACFA
ID   A4_MACFA       STANDARD;      PRT;   770 AA.
AC   P53601; Q95KN7;
DT   01-OCT-1996 (Rel. 34, Created)
DT   28-FEB-2003 (Rel. 41, Last sequence update)
DT   28-FEB-2003 (Rel. 41, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
GN   APP.
OS   Macaca fascicularis (Crab eating macaque) (Cynomolgus monkey).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Primates; Catarrhini; Cercopithecidae;
OC   Cercopithecinae; Macaca.
OX   NCBI_TaxID=9541;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORMS APP695 AND APP770).
RC   TISSUE=Cerebellum;
RX   MEDLINE=91273117; PubMed=1905108;
RA   Podlisny M.B., Tolan D.R., Selkoe D.J.;
RT   "Homology of the amyloid beta protein precursor in monkey and human
RT   supports a primate model for beta amyloidosis in Alzheimer's
RT   disease.";
RL   Am. J. Pathol. 138:1423-1435(1991).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction. In vitro, copper-metallated APP induces neuronal
CC       death directly or is potentiated through Cu(II)-mediated low-
CC       density lipoprotein oxidation (By similarity). Can regulate
CC       neurite outgrowth through binding to components of the
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CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity). The splice isoforms that contain the BPTI domain
CC       possess protease inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
CC       maturation occurs (O-glycosylated and sulfated). After alpha-
CC       secretase cleavage, soluble APP is released into the extracellular
CC       space and the C-terminal is internalized to endosomes and
CC       lysosomes. Some APP accumulates in secretory transport vesicles
CC       leaving the late Golgi compartment and returns to the cell
CC       surface. Gamma-CTF(59) peptide is located to both the cytoplasm
CC       and nuclei of neurons (By similarity).
CC   -!- ALTERNATIVE PRODUCTS:
CC       Event=Alternative splicing; Named isoforms=2;
CC         Comment=Additional isoforms seem to exist;
CC       Name=APP770;
CC         IsoId=P53601-1; Sequence=Displayed;
CC       Name=APP695;
CC         IsoId=P53601-2; Sequence=VSP_000010, VSP_000011;
CC   -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC       sorting of membrane proteins to the basolateral surface of
CC       epithelial cells (By similarity).
CC   -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC       phosphorylated proteins is required for the specific binding of
CC       the PID domain. However additional amino acids either N- or C-
CC       terminal to the NPXY motif are often required for complete
CC       interaction. The PID domain-containing proteins which bind APP
CC       require the YENPTY motif for full interaction. These interactions
CC       are independent of phosphorylation on the terminal tyrosine
CC       residue. The NPXY site is also involved in clathrin-mediated
CC       endocytosis (By similarity).
CC   -!- PTM: Proteolytically processed under normal cellular conditions.
CC       Cleavage by alpha-secretase or alternatively by beta-secretase
CC       leads to generation and extracellular release of soluble APP
CC       peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC       retention of corresponding membrane-anchored C-terminal fragments,
CC       C83 and C99. Subsequent processing of C83 by gamma-secretase
CC       yields P3 peptides. This is the major secretory pathway and is
CC       nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC       gamma-secretase processing of C99 releases the amyloid beta
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CC       proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC       major components of amyloid plaques, and the cytotoxic C-terminal
CC       fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
CC       similarity).
CC   -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC       (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC       results in the production of the neurotoxic C31 peptide and the
CC       increased production of beta-amyloid peptides (By similarity).
CC   -!- PTM: N- and O-glycosylated (By similarity).
CC   -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC       serine residues is neuron-specific. Phosphorylation can affect APP
CC       processing, neuronal differentiation and interaction with other
CC       proteins (By similarity).
CC   -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC       zinc, can induce histidine-bridging between beta-amyloid molecules
CC       resulting in beta-amyloid-metal aggregates (By similarity).
CC       Extracellular zinc-binding increases binding of heparin to APP and
CC       inhibits collagen-binding (By similarity).
CC   -!- SIMILARITY: Belongs to the APP family.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; M58727; AAA36829.1; -.
DR   EMBL; M58726; AAA36828.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Proteoglycan; Alternative splicing; Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    671       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       672    770       C99 (POTENTIAL).
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FT   CHAIN        672     713        BETA-AMYLOID PROTEIN 42 (POTENTIAL).
FT   CHAIN        672     711        BETA-AMYLOID PROTEIN 40 (POTENTIAL).
FT   CHAIN        688     770        C83 (POTENTIAL).
FT   CHAIN        688     713        P3(42) (POTENTIAL).
FT   CHAIN        688     711        P3(40) (POTENTIAL).
FT   CHAIN        712     770        GAMMA-CTF(59) (POTENTIAL).
FT   CHAIN        714     770        GAMMA-CTF(57) (POTENTIAL).
FT   CHAIN        721     770        GAMMA-CTF(50) (POTENTIAL).
FT   CHAIN        740     770        C31 (POTENTIAL).
FT   DOMAIN        18     699        EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     700     723        POTENTIAL.
FT   DOMAIN       724     770        CYTOPLASMIC (POTENTIAL).
FT   DOMAIN        96     110        HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       181     188        ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN       291     341        BPTI/KUNITZ INHIBITOR.
FT   DOMAIN       391     423        HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       491     522        HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN       523     540        COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN       732     751        INTERACTION WITH G(O)-ALPHA
FT                                   (BY SIMILARITY).
FT   DOMAIN       230     260        ASP/GLU-RICH (ACIDIC).
FT   DOMAIN       274     280        POLY-THR.
FT   SITE         144     144        REQUIRED FOR COPPER(II) REDUCTION
FT                                   (BY SIMILARITY).
FT   ACT_SITE     301     302        REACTIVE BOND (BY SIMILARITY).
FT   SITE         671     672        CLEAVAGE (BY BETA-SECRETASE)
FT                                   (BY SIMILARITY).
FT   SITE         672     673        CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
FT   SITE         687     688        CLEAVAGE (BY ALPHA-SECRETASE)
FT                                   (BY SIMILARITY).
FT   SITE         704     704        IMPLICATED IN FREE RADICAL PROPAGATION
FT                                   (BY SIMILARITY).
FT   SITE         706     706        INVOLVED IN OXIDATIVE REACTIONS
FT                                   (BY SIMILARITY).
FT   SITE         711     712        CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                   (BY SIMILARITY).
FT   SITE         713     714        CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                   (BY SIMILARITY).
FT   SITE         720     721        CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)
FT                                   (BY SIMILARITY).
FT   SITE         724     734        BASOLATERAL SORTING SIGNAL
FT                                   (BY SIMILARITY).
FT   SITE         739     740        CLEAVAGE (BY CASPASES-3,-6,-8 OR -9)

  Query Match             85.4%;  Score 35;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694


RESULT 10
A4_MOUSE
ID   A4_MOUSE       STANDARD;      PRT;   770 AA.
AC   P12023; P97487; P97942; Q99K32;
```

```
DT   01-OCT-1989 (Rel. 12, Created)
DT   10-OCT-2003 (Rel. 42, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains:
DE   Soluble APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99
DE   (APP-C99); Beta-amyloid protein 42 (Beta-APP42); Beta-amyloid protein
DE   40 (Beta-APP40); C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase
DE   C-terminal fragment 59) (Amyloid intracellular domain 59) (AID(59))
DE   (APP-C59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57)
DE   (Amyloid intracellular domain 57) (AID(57)) (APP-C57); Gamma-CTF(50)
DE   (Gamma-secretase C-terminal fragment 50) (Amyloid intracellular domain
DE   50) (AID(50)); C31].
GN   APP.
OS   Mus musculus (Mouse).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus.
OX   NCBI_TaxID=10090;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88106489; PubMed=3322280;
RA   Yamada T., Sasaki H., Furuya H., Miyata T., Goto I., Sakaki Y.;
RT   "Complementary DNA for the mouse homolog of the human amyloid beta
RT   protein precursor.";
RL   Biochem. Biophys. Res. Commun. 149:665-671(1987).
RN   [2]
RP   REVISIONS.
RA   Yamada T.;
RL   Submitted (MAR-1988) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=BALB/c; TISSUE=Brain;
RX   MEDLINE=92096458; PubMed=1756177;
RA   de Strooper B., van Leuven F., van den Berghe H.;
RT   "The amyloid beta protein precursor or proteinase nexin II from mouse
RT   is closer related to its human homolog than previously reported.";
RL   Biochim. Biophys. Acta 1129:141-143(1991).
RN   [4]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   STRAIN=SAMP8; TISSUE=Hippocampus;
RX   MEDLINE=21130647; PubMed=11235921;
RA   Kumar V.B., Vyas K., Franko M., Choudhary V., Buddhiraju C.,
RA   Alvarez J., Morley J.E.;
RT   "Molecular cloning, expression, and regulation of hippocampal amyloid
RT   precursor protein of senescence accelerated mouse (SAMP8).";
RL   Biochem. Cell Biol. 79:57-67(2001).
RN   [5]
RP   SEQUENCE OF 1-19 FROM N.A.
RX   MEDLINE=92209998; PubMed=1555768;
RA   Izumi R., Yamada T., Yoshikai S.I., Sasaki H., Hattori M.,
RA   Sakai Y.;
RT   "Positive and negative regulatory elements for the expression of the
RT   Alzheimer's disease amyloid precursor-encoding gene in mouse.";
RL   Gene 112:189-195(1992).
RN   [6]
RP   PARTIAL SEQUENCE FROM N.A. (ISOFORM APP770).
```

RC TISSUE=Breast tumor;
RX MEDLINE=22388257; PubMed=12477932;
RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,
RA Klausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
RA Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
RA Hopkins R.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,
RA Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
RA Stapleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
RA Bosak S.A., McEwan P.J., McKernan K.J., Malek J.A., Gunaratne P.H.,
RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,
RA Villalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A.,
RA Fahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,
RA Whiting M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
RA Blakesley R.W., Touchman J.W., Green E.D., Dickson M.C.,
RA Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
RA Butterfield Y.S.N., Krzywinski M.I., Skalska U., Smailus D.E.,
RA Schnerch A., Schein J.E., Jones S.J.M., Marra M.A.;
RT "Generation and initial analysis of more than 15,000 full-length human
RT and mouse cDNA sequences.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002).
RN [7]
RP SEQUENCE OF 281-380 FROM N.A., AND ALTERNATIVE SPLICING.
RC TISSUE=Brain, and Kidney;
RX MEDLINE=89149813; PubMed=2493250;
RA Yamada T., Sasaki H., Dohura K., Goto I., Sakaki Y.;
RT "Structure and expression of the alternatively-spliced forms of mRNA
RT for the mouse homolog of Alzheimer's disease amyloid beta protein
RT precursor.";
RL Biochem. Biophys. Res. Commun. 158:906-912(1989).
RN [8]
RP SEQUENCE OF 289-364 FROM N.A.
RC STRAIN=CD-1; TISSUE=Placenta;
RX MEDLINE=89345111; PubMed=2569710;
RA Fukuchi K., Martin G.M., Deeb S.S.;
RT "Sequence of the protease inhibitor domain of the A4 amyloid protein
RT precursor of Mus domesticus.";
RL Nucleic Acids Res. 17:5396-5396(1989).
RN [9]
RP SEQUENCE OF 656-737 FROM N.A.
RC STRAIN=129/Sv;
RA Wragg M.A., Busfield F., Duff K., Korenblat K., Capecchi M.,
RA Loring J.F., Goate A.M.;
RT "Introduction of six mutations into the mouse genome using 'Hit and
RT Run' gene-targeting: introduction of familial Alzheimer's disease
RT mutations into the mouse amyloid precursor protein gene and
RT humanization of the A-beta fragment.";
RL Submitted (DEC-1996) to the EMBL/GenBank/DDBJ databases.
RN [10]
RP TISSUE SPECIFICITY OF ALTERNATIVE SPLICED FORMS.
RX MEDLINE=93287808; PubMed=8510506;
RA Sola C., Mengod G., Ghetti B., Palacios J.M., Triarhou L.C.;
RT "Regional distribution of the alternatively spliced isoforms of beta
RT APP RNA transcript in the brain of normal, heterozygous and
RT homozygous weaver mutant mice as revealed by in situ hybridization
RT histochemistry.";

RL Brain Res. Mol. Brain Res. 17:340-346(1993).
RN [11]
RP INTERACTION WITH KNS2.
RX MEDLINE=21010507; PubMed=11144355;
RA Kamal A., Stokin G.B., Yang Z., Xia C.-H., Goldstein L.S.;
RT "Axonal transport of amyloid precursor protein is mediated by direct
RT binding to the kinesin light chain subunit of kinesin-I.";
RL Neuron 28:449-459(2000).
RN [12]
RP C-TERMINAL PROTEIN-PROTEIN INTERACTIONS, AND MUTAGENESIS OF TYR-728;
RP THR-743; TYR-757; ASN-759 AND TYR-762.
RX MEDLINE=21408156; PubMed=11517249;
RA Matsuda S., Yasukawa T., Homma Y., Ito Y., Niikura T., Hiraki T.,
RA Hirai S., Ohno S., Kita Y., Kawasumi M., Kouyama K., Yamamoto T.,
RA Kyriakis J.M., Nishimoto I.;
RT "C-jun N-terminal kinase (JNK)-interacting protein-1b/islet-brain-1
RT scaffolds Alzheimer's amyloid precursor protein with JNK.";
RL J. Neurosci. 21:6597-6607(2001).
RN [13]
RP INTERACTION WITH MAPK8IP1, AND PHOSPHORYLATION.
RX MEDLINE=22028091; PubMed=11912189;
RA Taru H., Iijima K.-I., Hase M., Kirino Y., Yagi Y., Suzuki T.;
RT "Interaction of Alzheimer's beta-amyloid precursor family proteins
RT with scaffold proteins of the JNK signaling cascade.";
RL J. Biol. Chem. 277:20070-20078(2002).
RN [14]
RP INTERACTION OF CTF PEPTIDES WITH NUMB.
RX MEDLINE=22008109; PubMed=12011466;
RA Roncarati R., Sestan N., Scheinfeld M.H., Berechid B.E., Lopez P.A.,
RA Meucci O., McGlade J.C., Rakic P., D'Adamio L.;
RT "The gamma-secretase-generated intracellular domain of beta-amyloid
RT precursor protein binds Numb and inhibits Notch signaling.";
RL Proc. Natl. Acad. Sci. U.S.A. 99:7102-7107(2002).
RN [15]
RP GAMMA-SECRETASE PROCESSING, AND INTERACTION WITH APBB1.
RX MEDLINE=21437805; PubMed=11553691;
RA Cupers P., Orlans I., Craessaerts K., Annaert W., De Strooper B.;
RT "The amyloid precursor protein (APP)-cytoplasmic fragment generated by
RT gamma-secretase is rapidly degraded but distributes partially in a
RT nuclear fraction of neurones in culture.";
RL J. Neurochem. 78:1168-1178(2001).
CC -!- FUNCTION: Functions as a cell surface receptor and performs
CC physiological functions on the surface of neurons relevant to
CC neurite growth, neuronal adhesion and axonogenesis. Involved in
CC cell mobility and transcription regulation through protein-protein
CC interactions. Can promote transcription activation through binding
CC to APBB1/Tip60 and inhibit Notch signaling through interaction
CC with Numb. Couples to apoptosis-inducing pathways such as those
CC mediated by G(O) and JIP. Inhibits G(O) alpha ATPase activity (By
CC similarity). Acts as a kinesin I membrane receptor, mediating the
CC axonal transport of beta-secretase and presenilin 1. May be
CC involved in copper homeostasis/oxidative stress through copper ion
CC reduction. Can regulate neurite outgrowth through binding to
CC components of the extracellular matrix such as heparin and
CC collagen I and IV (By similarity). The splice isoforms that
CC contain the BPTI domain possess protease inhibitor activity (By
CC similarity).

```
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC       only weakly transient metals and have little reducing activity due
CC       to substitutions of transient metal chelating residues. Beta-APP42
CC       may activate mononuclear phagocytes in the brain and elicit
CC       inflammatory responses. Promotes both tau aggregation and TPK II-
CC       mediated phosphorylation (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis.
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1, Numb and Dab1. Binding to Dab1 inhibits
CC       its serine phosphorylation. Also interacts with GPCR-like protein
CC       BPP, FPRL1, APPBP1, IB1, KNS2 (via its TPR domains), APPBP2 (via
CC       BaSS) and DDB1 (By similarity). In vitro, it binds MAPT via the
CC       MT-binding domains (By similarity). Associates with microtubules
CC       in the presence of ATP and in a kinesin-dependent manner (By
CC       similarity). Interacts, through a C-terminal domain, with GNAO1
CC       (By similarity). Amyloid beta-42 binds CHRNA7 in hippocampal
CC       neurons (By similarity). Beta-amyloid associates with HADH2 (By
CC       similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
```

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  Query Match             85.4%;  Score 35;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694
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RESULT 11
A4_PIG
ID   A4_PIG          STANDARD;      PRT;   770 AA.
AC   P79307; Q29023; Q9TUI0;
DT   01-NOV-1997 (Rel. 35, Created)
DT   10-OCT-2003 (Rel. 42, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (ABPP) (Alzheimer's disease
DE   amyloid protein homolog) [Contains: Soluble APP-alpha (S-APP-alpha);
DE   Soluble APP-beta (S-APP-beta); C99; Beta-amyloid protein 42 (Beta-
DE   APP42); Beta-amyloid protein 40 (Beta-APP40); C83; P3(42); P3(40);
DE   Gamma-CTF(59) (Gamma-secretase C-terminal fragment 59); Gamma-CTF(57)
DE   (Gamma-secretase C-terminal fragment 57); Gamma-CTF(50) (Gamma-
DE   secretase C-terminal fragment 50); C31].
OS   Sus scrofa (Pig).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Suina; Suidae; Sus.
OX   NCBI_TaxID=9823;
RN   [1]
RP   SEQUENCE FROM N.A.
```

```
RA   Kimura A., Takahashi T.;
RT   "Amyloid precursor protein 770.";
RL   Submitted (SEP-1999) to the EMBL/GenBank/DDBJ databases.
RN   [2]
RP   SEQUENCE OF 1-136 FROM N.A.
RC   TISSUE=Small intestine;
RA   Winteroe A.K., Fredholm M.;
RT   "Evaluation and characterization of a porcine small intestine cDNA
RT   library.";
RL   Submitted (JAN-1997) to the EMBL/GenBank/DDBJ databases.
RN   [3]
RP   SEQUENCE OF 667-723 FROM N.A.
RC   TISSUE=Brain;
RX   MEDLINE=92017079; PubMed=1656157;
RA   Johnstone E.M., Chaney M.O., Norris F.H., Pascual R., Little S.P.;
RT   "Conservation of the sequence of the Alzheimer's disease amyloid
RT   peptide in dog, polar bear and five other mammals by cross-species
RT   polymerase chain reaction analysis.";
RL   Brain Res. Mol. Brain Res. 10:299-305(1991).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP (By
CC       similarity). Inhibits G(0) alpha ATPase activity (By similarity).
CC       Acts as a kinesin I membrane receptor, mediating the axonal
CC       transport of beta-secretase and presenilin 1 (By similarity). May
CC       be involved in copper homeostasis/oxidative stress through copper
CC       ion reduction (By similarity). In vitro, copper-metallated APP
CC       induces neuronal death directly or is potentiated through Cu(II)-
CC       mediated low-density lipoprotein oxidation (By similarity). Can
CC       regulate neurite outgrowth through binding to components of the
CC       extracellular matrix such as heparin and collagen I and IV (By
CC       similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron (By similarity).
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, and SHC1, Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains) (By similarity), APPBP2 (via BaSS) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the
CC       endoplasmic reticulum) moves to the Golgi complex where complete
CC       maturation occurs (O-glycosylated and sulfated). After alpha-
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CC secretase cleavage, soluble APP is released into the extracellular
CC space and the C-terminal is internalized to endosomes and
CC lysosomes. Some APP accumulates in secretory transport vesicles
CC leaving the late Golgi compartment and returns to the cell
CC surface. Gamma-CTF(59) peptide is located to both the cytoplasm
CC and nuclei of neurons (By similarity).
CC -!- DOMAIN: The basolateral sorting signal (BaSS) is required for
CC sorting of membrane proteins to the basolateral surface of
CC epithelial cells (By similarity).
CC -!- DOMAIN: The NPXY sequence motif found in many tyrosine-
CC phosphorylated proteins is required for the specific binding of
CC the PID domain. However additional amino acids either N- or C-
CC terminal to the NPXY motif are often required for complete
CC interaction. The PID domain-containing proteins which bind APP
CC require the YENPTY motif for full interaction. These interactions
CC are independent of phosphorylation on the terminal tyrosine
CC residue. The NPXY site is also involved in clathrin-mediated
CC endocytosis (By similarity).
CC -!- PTM: Proteolytically processed under normal cellular conditions.
CC Cleavage by alpha-secretase or alternatively by beta-secretase
CC leads to generation and extracellular release of soluble APP
CC peptides, S-APP-alpha and S-APP-beta, respectively, and the
CC retention of corresponding membrane-anchored C-terminal fragments,
CC C83 and C99. Subsequent processing of C83 by gamma-secretase
CC yields P3 peptides. This is the major secretory pathway and is
CC nonamyloidogenic. Alternatively, presenilin/nicastrin-mediated
CC gamma-secretase processing of C99 releases the amyloid beta
CC proteins, amyloid-beta 40 (Abeta40) and amyloid-beta 42 (Abeta42),
CC major components of amyloid plaques, and the cytotoxic C-terminal
CC fragments, gamma-CTF(50), gamma-CTF(57) and gamma-CTF(59) (By
CC similarity).
CC -!- PTM: Proteolytically cleaved by caspases during neuronal apoptosis
CC (By similarity). Cleavage at Asp-739 by either caspase-3, -8 or -9
CC results in the production of the neurotoxic C31 peptide and the
CC increased production of beta-amyloid peptides (By similarity).
CC -!- PTM: N- and O-glycosylated (By similarity).
CC -!- PTM: Phosphorylation in the C-terminal on tyrosine, threonine and
CC serine residues is neuron-specific. Phosphorylation can affect APP
CC processing, neuronal differentiation and interaction with other
CC proteins (By similarity).
CC -!- PTM: Extracellular binding and reduction of copper, results in a
CC corresponding oxidation of Cys-144 and Cys-158, and the formation
CC of a disulfide bond (By similarity).
CC -!- MISCELLANEOUS: Chelation of metal ions, notably copper, iron and
CC zinc, can induce histidine-bridging between beta-amyloid molecules
CC resulting in beta-amyloid-metal aggregates (By similarity).
CC Extracellular zinc-binding increases binding of heparin to APP and
CC inhibits collagen-binding (By similarity).
CC -!- SIMILARITY: Belongs to the APP family.
CC -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC ---

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CC   or send an email to license@isb-sib.ch).
CC   -----------------------------------------------------------------------
DR   EMBL; AB032550; BAA84580.1; -.
DR   EMBL; Z84022; CAB06313.1; -.
DR   EMBL; X56127; CAA39592.1; -.
DR   HSSP; P05067; 1AAP.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Apoptosis; Endocytosis; Cell adhesion; Serine protease inhibitor;
KW   Coated pits; Neurone; Heparin-binding; Metal-binding; Copper; Iron;
KW   Zinc; Signal; Transmembrane; Glycoprotein; Phosphorylation;
KW   Amyloid.
FT   SIGNAL        1     17       BY SIMILARITY.
FT   CHAIN        18    770       AMYLOID BETA A4 PROTEIN.
FT   CHAIN        18    687       SOLUBLE APP-ALPHA (POTENTIAL).
FT   CHAIN        18    671       SOLUBLE APP-BETA (POTENTIAL).
FT   CHAIN       672    770       C99 (BY SIMILARITY).
FT   CHAIN       672    713       BETA-AMYLOID PROTEIN 42 (BY SIMILARITY).
FT   CHAIN       672    711       BETA-AMYLOID PROTEIN 40 (BY SIMILARITY).
FT   CHAIN       688    770       C83 (BY SIMILARITY).
FT   CHAIN       688    713       P3(42) (BY SIMILARITY).
FT   CHAIN       688    711       P3(40) (BY SIMILARITY).
FT   CHAIN       712    770       GAMMA-CTF(59).
FT   CHAIN       714    770       GAMMA-CTF(57).
FT   CHAIN       721    770       GAMMA-CTF(50) (BY SIMILARITY).
FT   CHAIN       740    770       C31 (DURING APOPTOSIS) (BY SIMILARITY).
FT   DOMAIN       18    699       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    700    723       POTENTIAL.
FT   DOMAIN      724    770       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN       96    110       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      135    155       COPPER-BINDING (BY SIMILARITY).
FT   DOMAIN      181    188       ZINC-BINDING (BY SIMILARITY).
FT   DOMAIN      291    341       BPTI/KUNITZ INHIBITOR.
FT   DOMAIN      391    423       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      491    522       HEPARIN-BINDING (BY SIMILARITY).
FT   DOMAIN      523    540       COLLAGEN-BINDING (BY SIMILARITY).
FT   DOMAIN      732    751       INTERACTION WITH G(O)-ALPHA (BY
FT                                SIMILARITY).
FT   DOMAIN      230    260       ASP/GLU-RICH (ACIDIC).
FT   DOMAIN      274    280       POLY-THR.
FT   SITE        144    144       REQUIRED FOR COPPER(II) REDUCTION
FT                                (BY SIMILARITY).
FT   ACT_SITE    301    302       REACTIVE BOND (BY SIMILARITY).
FT   SITE        671    672       CLEAVAGE (BY BETA-SECRETASE)
FT                                (BY SIMILARITY).
FT   SITE        672    673       CLEAVAGE (BY CASPASE-6) (BY SIMILARITY).
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FT   SITE        687    688       CLEAVAGE (BY ALPHA-SECRETASE)
FT                                (BY SIMILARITY).
FT   SITE        704    704       IMPLICATED IN FREE RADICAL PROPAGATION
FT                                (BY SIMILARITY).
FT   SITE        706    706       INVOLVED IN OXIDATIVE REACTIONS
FT                                (BY SIMILARITY).
FT   SITE        711    712       CLEAVAGE (BY GAMMA-SECRETASE; SITE 1)
FT                                (BY SIMILARITY).
FT   SITE        713    714       CLEAVAGE (BY GAMMA-SECRETASE; SITE 2)
FT                                (BY SIMILARITY).
FT   SITE        720    721       CLEAVAGE (BY GAMMA-SECRETASE; SITE 3)

  Query Match             85.4%;  Score 35;  DB 1;  Length 770;
  Best Local Similarity   100.0%;  Pred. No. 9.8;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694


RESULT 12
A4_RAT
ID   A4_RAT          STANDARD;      PRT;   770 AA.
AC   P08592;
DT   01-AUG-1988 (Rel. 08, Created)
DT   01-DEC-1992 (Rel. 24, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Amyloid beta A4 protein precursor (APP) (Alzheimer's disease amyloid
DE   protein homolog) (Amyloidogenic glycoprotein) (AG) [Contains: Soluble
DE   APP-alpha (S-APP-alpha); Soluble APP-beta (S-APP-beta); C99; Beta-
DE   amyloid protein 42 (Beta-APP42); Beta-amyloid protein 40 (Beta-APP40);
DE   C83; P3(42); P3(40); Gamma-CTF(59) (Gamma-secretase C-terminal
DE   fragment 59); Gamma-CTF(57) (Gamma-secretase C-terminal fragment 57);
DE   Gamma-CTF(50) (Gamma-secretase C-terminal fragment 50); C31].
GN   APP.
OS   Rattus norvegicus (Rat).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Rattus.
OX   NCBI_TaxID=10116;
RN   [1]
RP   SEQUENCE FROM N.A. (ISOFORM APP695).
RC   TISSUE=Brain;
RX   MEDLINE=88312583; PubMed=2900758;
RA   Shivers B.D., Hilbich C., Multhaup G., Salbaum J.M., Beyreuther K.,
RA   Seeburg P.H.;
RT   "Alzheimer's disease amyloidogenic glycoprotein: expression pattern
RT   in rat brain suggests a role in cell contact.";
RL   EMBO J. 7:1365-1370(1988).
RN   [2]
RP   SEQUENCE OF 289-364 FROM N.A.
RC   TISSUE=Liver;
RX   MEDLINE=89183625; PubMed=2648331;
RA   Kang J., Mueller-Hill B.;
RT   "The sequence of the two extra exons in rat preA4.";
RL   Nucleic Acids Res. 17:2130-2130(1989).
RN   [3]
```

RP SEQUENCE OF 720-730, AND MASS SPECTROMETRY.
RX MEDLINE=21443797; PubMed=11483588;
RA Gu Y., Misonou H., Sato T., Dohmae N., Takio K., Ihara Y.;
RT "Distinct intramembrane cleavage of the beta-amyloid precursor protein
RT family resembling gamma-secretase-like cleavage of Notch.";
RL J. Biol. Chem. 276:35235-35238(2001).
RN [4]
RP ALTERNATIVE SPLICING.
RX MEDLINE=96187032; PubMed=8624099;
RA Sandbrink R., Masters C.L., Beyreuther K.;
RT "APP gene family. Alternative splicing generates functionally related
RT isoforms.";
RL Ann. N.Y. Acad. Sci. 777:281-287(1996).
RN [5]
RP TISSUE SPECIFICITY OF APPICAN.
RX MEDLINE=95263526; PubMed=7744833;
RA Shioi J., Pangalos M.N., Ripellino J.A., Vassilacopoulou D.,
RA Mytilineou C., Margolis R.U., Robakis N.K.;
RT "The Alzheimer amyloid precursor proteoglycan (appican) is present in
RT brain and is produced by astrocytes but not by neurons in primary
RT neural cultures.";
RL J. Biol. Chem. 270:11839-11844(1995).
RN [6]
RP TISSUE SPECIFICITY OF ISOFORMS.
RX MEDLINE=97150061; PubMed=8996834;
RA Sandbrink R., Monning U., Masters C.L., Beyreuther K.;
RT "Expression of the APP gene family in brain cells, brain development
RT and aging.";
RL Gerontology 43:119-131(1997).
RN [7]
RP INTERACTION WITH DDB1, AND MUTAGENESIS OF TYR-757; ASN-759 AND
RP TYR-762.
RX MEDLINE=99127916; PubMed=9930726;
RA Watanabe T., Sukegawa J., Tomita S., Iijima K.-I., Oguchi S.,
RA Suzuki T., Nairn A.C., Greengard P.;
RT "A 127-kDa protein (UV-DDB) binds to the cytoplasmic domain of the
RT Alzheimer's amyloid precursor protein.";
RL J. Neurochem. 72:549-556(1999).
RN [8]
RP INTERACTION WITH GNAO1, AND MUTAGENESIS OF 732-HIS-HIS-733.
RX MEDLINE=99162676; PubMed=10024358;
RA Brouillet E., Trembleau A., Galanaud D., Volovitch M., Bouillot C.,
RA Valenza C., Prochiantz A., Allinquant B.;
RT "The amyloid precursor protein interacts with Go heterotrimeric
RT protein within a cell compartment specialized in signal
RT transduction.";
RL J. Neurosci. 19:1717-1727(1999).
RN [9]
RP CHARACTERISTICS OF APPICAN, AND MUTAGENESIS OF SER-656.
RX MEDLINE=95256193; PubMed=7737970;
RA Pangalos M.N., Efthimiopoulos S., Shioi J., Robakis N.K.;
RT "The chondroitin sulfate attachment site of appican is formed by
RT splicing out exon 15 of the amyloid precursor gene.";
RL J. Biol. Chem. 270:10388-10391(1995).
RN [10]
RP BETA-AMYLOID METAL-BINDING.
RX MEDLINE=99316162; PubMed=10386999;

RA Huang X., Atwood C.S., Hartshorn M.A., Multhaup G., Goldstein L.E.,
RA Scarpa R.C., Cuajungco M.P., Gray D.N., Lim J., Moir R.D., Tanzi R.E.,
RA Bush A.I.;
RT "The A beta peptide of Alzheimer's disease directly produces hydrogen
RT peroxide through metal ion reduction.";
RL Biochemistry 38:7609-7616(1999).
RN [11]
RP BETA-AMYLOID ZINC BINDING.
RX MEDLINE=99343552; PubMed=10413512;
RA Liu S.T., Howlett G., Barrow C.J.;
RT "Histidine-13 is a crucial residue in the zinc ion-induced aggregation
RT of the A beta peptide of Alzheimer's disease.";
RL Biochemistry 38:9373-9378(1999).
RN [12]
RP IMPORTANCE OF GLY-704 IN FREE RADICAL PROPAGATION, AND MUTAGENESIS OF
RP GLY-704.
RX MEDLINE=21956095; PubMed=11959460;
RA Kanski J., Varadarajan S., Aksenova M., Butterfield D.A.;
RT "Role of glycine-33 and methionine-35 in Alzheimer's amyloid beta-
RT peptide 1-42-associated oxidative stress and neurotoxicity.";
RL Biochim. Biophys. Acta 1586:190-198(2001).
RN [13]
RP PHOSPHORYLATION.
RX MEDLINE=97239592; PubMed=9085254;
RA Oishi M., Nairn A.C., Czernik A.J., Lim G.S., Isohara T., Gandy S.E.,
RA Greengard P., Suzuki T.;
RT "The cytoplasmic domain of Alzheimer's amyloid precursor protein is
RT phosphorylated at Thr654, Ser655, and Thr668 in adult rat brain and
RT cultured cells.";
RL Mol. Med. 3:111-123(1997).
RN [14]
RP PHOSPHORYLATION ON SER-730.
RX MEDLINE=99262094; PubMed=10329382;
RA Isohara T., Horiuchi A., Watanabe T., Ando K., Czernik A.J., Uno I.,
RA Greengard P., Nairn A.C., Suzuki T.;
RT "Phosphorylation of the cytoplasmic domain of Alzheimer's beta-amyloid
RT precursor protein at Ser655 by a novel protein kinase.";
RL Biochem. Biophys. Res. Commun. 258:300-305(1999).
RN [15]
RP PHOSPHORYLATION, INDUCTION, SUBCELLULAR LOCATION, AND MUTAGENESIS OF
RP THR-743.
RX MEDLINE=99274744; PubMed=10341243;
RA Ando K., Oishi M., Takeda S., Iijima K.-I., Isohara T., Nairn A.C.,
RA Kirino Y., Greengard P., Suzuki T.;
RT "Role of phosphorylation of Alzheimer's amyloid precursor protein
RT during neuronal differentiation.";
RL J. Neurosci. 19:4421-4427(1999).
RN [16]
RP PHOSPHORYLATION ON THR-743.
RX MEDLINE=20396183; PubMed=10936190;
RA Iijima K.-I., Ando K., Takeda S., Satoh Y., Seki T., Itohara S.,
RA Greengard P., Kirino Y., Nairn A.C., Suzuki T.;
RT "Neuron-specific phosphorylation of Alzheimer's beta-amyloid precursor
RT protein by cyclin-dependent kinase 5.";
RL J. Neurochem. 75:1085-1091(2000).
RN [17]
RP CARBOHYDRATE STRUCTURE OF APPICAN.

```
RX   MEDLINE=21463085; PubMed=11479316;
RA   Tsuchida K., Shioi J., Yamada S., Boghosian G., Wu A., Cai H.,
RA   Sugahara K., Robakis N.K.;
RT   "Appican, the proteoglycan form of the amyloid precursor protein,
RT   contains chondroitin sulfate E in the repeating disaccharide region
RT   and 4-O-sulfated galactose in the linkage region.";
RL   J. Biol. Chem. 276:37155-37160(2001).
CC   -!- FUNCTION: Functions as a cell surface receptor and performs
CC       physiological functions on the surface of neurons relevant to
CC       neurite growth, neuronal adhesion and axonogenesis. Involved in
CC       cell mobility and transcription regulation through protein-protein
CC       interactions (By similarity). Can promote transcription activation
CC       through binding to APBB1/Tip60 and inhibit Notch signaling through
CC       interaction with Numb (By similarity). Couples to apoptosis-
CC       inducing pathways such as those mediated by G(O) and JIP. Inhibits
CC       G(O) alpha ATPase activity. Acts as a kinesin I membrane receptor,
CC       mediating the axonal transport of beta-secretase and presenilin 1
CC       (By similarity). May be involved in copper homeostasis/oxidative
CC       stress through copper ion reduction. Can regulate neurite
CC       outgrowth through binding to components of the extracellular
CC       matrix such as heparin and collagen I and IV (By similarity). The
CC       splice isoforms that contain the BPTI domain possess protease
CC       inhibitor activity (By similarity).
CC   -!- FUNCTION: Beta-amyloid peptides are lipophilic metal chelators
CC       with metal-reducing activity. Bind transient metals such as
CC       copper, zinc and iron. Rat and mouse beta-amyloid peptides bind
CC       only weakly transient metals and have little reducing activity due
CC       to substitutions of transient metal chelating residues. Beta-APP42
CC       may activate mononuclear phagocytes in the brain and elicit
CC       inflammatory responses. Promotes both tau aggregation and TPK II-
CC       mediated phosphorylation (By similarity).
CC   -!- FUNCTION: Appicans elicit adhesion of neural cells to the
CC       extracellular matrix and may regulate neurite outgrowth in the
CC       brain.
CC   -!- FUNCTION: The gamma-CTF peptides as well as the caspase-cleaved
CC       peptides, including C31, are potent enhancers of neuronal
CC       apoptosis (By similarity).
CC   -!- SUBUNIT: Binds, via its C-terminal, to the PID domain of several
CC       cytoplasmic proteins, including APBB family members, the APBA
CC       family, MAPK8IP1, SHC1 and Numb and Dab1 (By similarity). Binding
CC       to Dab1 inhibits its serine phosphorylation (By similarity). Also
CC       interacts with GPCR-like protein BPP, FPRL1, APPBP1, IB1, KNS2
CC       (via its TPR domains), APPBP2 (via BaSS) (By similarity) and DDB1.
CC       In vitro, it binds MAPT via the MT-binding domains (By
CC       similarity). Associates with microtubules in the presence of ATP
CC       and in a kinesin-dependent manner (By similarity). Interacts,
CC       through a C-terminal domain, with GNAO1. Amyloid beta-42 binds
CC       CHRNA7 in hippocampal neurons (By similarity). Beta-amyloid
CC       associates with HADH2 (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein. Cell surface
CC       protein that rapidly becomes internalized via clathrin-coated
CC       pits. During maturation, the immature APP (N-glycosylated in the

Query Match             85.4%;  Score 35;  DB 1;  Length 770;
Best Local Similarity   100.0%;  Pred. No. 9.8;
Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;
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Qy          1 LVFFAED 7
              |||||||
Db        688 LVFFAED 694


RESULT 13
A4_TETFL
ID   A4_TETFL       STANDARD;      PRT;   780 AA.
AC   O73683;
DT   10-OCT-2003 (Rel. 42, Created)
DT   10-OCT-2003 (Rel. 42, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog precursor [Contains:
DE   Beta-amyloid protein (Beta-APP) (A-beta)].
GN   APP.
OS   Tetraodon fluviatilis (Puffer fish).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
OC   Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;
OC   Tetradontoidea; Tetraodontidae; Tetraodon.
OX   NCBI_TaxID=47145;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98252138; PubMed=9599080;
RA   Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;
RT   "Analysis of pufferfish homologues of the AT-rich human APP gene.";
RL   Gene 210:17-24(1998).
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ----------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ----------------------------------------------------------------------
DR   EMBL; AF018165; AAC41275.1; -.
DR   HSSP; P05067; 1HZ3.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; 1.
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DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; FALSE_NEG.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;
KW   Serine protease inhibitor.
FT   SIGNAL        1     18       POTENTIAL.
FT   CHAIN        19    780       ALZHEIMER'S DISEASE AMYLOID A4 PROTEIN
FT                                 HOMOLOG.
FT   CHAIN       682    724       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       19    711       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    712    732       POTENTIAL.
FT   DOMAIN      733    780       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN      323    382       BPTI/KUNITZ INHIBITOR.
FT   SITE        769    772       CLATHRIN-BINDING (BY SIMILARITY).
FT   DISULFID    327    378       BY SIMILARITY.
FT   DISULFID    336    361       BY SIMILARITY.
FT   CARBOHYD    560    560       N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ   SEQUENCE   780 AA;  88238 MW;  60071BE94520191D CRC64;

  Query Match             85.4%;  Score 35;  DB 1;  Length 780;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||||
Db        698 LVFFAED 704


RESULT 14
PE23_SHEEP
ID   PE23_SHEEP     STANDARD;      PRT;     89 AA.
AC   Q28550;
DT   01-NOV-1997 (Rel. 35, Created)
DT   01-NOV-1997 (Rel. 35, Last sequence update)
DT   15-MAR-2004 (Rel. 43, Last annotation update)
DE   Prostaglandin E2 receptor, EP3 subtype (Prostanoid EP3 receptor) (PGE
DE   receptor, EP3 subtype) (Fragment).
GN   PTGER3.
OS   Ovis aries (Sheep).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Mammalia; Eutheria; Cetartiodactyla; Ruminantia; Pecora; Bovoidea;
OC   Bovidae; Caprinae; Ovis.
OX   NCBI_TaxID=9940;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   TISSUE=Kidney outer medulla;
RX   MEDLINE=98287159; PubMed=9625477;
RA   Audicana L., Aughey E., O'Shaughnessy P.J.;
RT   "Sensitivity of the early luteal phase ovine cervix to prostaglandin
RT   E2 (PGE2) and expression of EP3 receptor mRNA.";
RL   Res. Vet. Sci. 64:177-179(1998).
CC   -!- FUNCTION: Receptor for prostaglandin E2 (PGE2); the EP3 receptor
CC       may be involved in inhibition of gastric acid secretion,
CC       modulation of neurotransmitter release in central and peripheral
CC       neurons, inhibition of sodium and water reabsorption in kidney
CC       tubulus and contraction in uterine smooth muscle. The activity of
CC       this receptor can couple to both the inhibition of adenylate
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CC       cyclase mediated by G(i) proteins, and to an elevation of
CC       intracellular calcium (By similarity).
CC   -!- SUBCELLULAR LOCATION: Integral membrane protein.
CC   -!- SIMILARITY: Belongs to family 1 of G-protein coupled receptors.
CC   ---------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
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CC   use by non-profit institutions as long as its content is in no way
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CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------
DR   EMBL; U37148; AAB81195.1; -.
DR   InterPro; IPR000276; GPCR_Rhodpsn.
DR   PROSITE; PS00237; G_PROTEIN_RECEP_F1_1; FALSE_NEG.
KW   G-protein coupled receptor; Transmembrane; Glycoprotein.
FT   NON_TER       1      1
FT   TRANSMEM     <1     18       4 (POTENTIAL).
FT   DOMAIN       19     48       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM     49     74       5 (POTENTIAL).
FT   DOMAIN       75     89       CYTOPLASMIC (POTENTIAL).
FT   CARBOHYD     38     38       N-LINKED (GLCNAC. . .) (POTENTIAL).
FT   NON_TER      89     89
SQ   SEQUENCE   89 AA;  9364 MW;  EDAD27E127B0A428 CRC64;

  Query Match             78.0%;  Score 32;  DB 1;  Length 89;
  Best Local Similarity   85.7%;  Pred. No. 5.1;
  Matches    6;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          2 VFFAEDF 8
              |||| ||
Db         49 VFFASDF 55


RESULT 15
A4_FUGRU
ID   A4_FUGRU       STANDARD;      PRT;   737 AA.
AC   O93279;
DT   10-OCT-2003 (Rel. 42, Created)
DT   10-OCT-2003 (Rel. 42, Last sequence update)
DT   10-OCT-2003 (Rel. 42, Last annotation update)
DE   Alzheimer's disease amyloid A4 protein homolog precursor [Contains:
DE   Beta-amyloid protein (Beta-APP) (A-beta)].
GN   APP.
OS   Fugu rubripes (Japanese pufferfish) (Takifugu rubripes).
OC   Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
OC   Actinopterygii; Neopterygii; Teleostei; Euteleostei; Neoteleostei;
OC   Acanthomorpha; Acanthopterygii; Percomorpha; Tetraodontiformes;
OC   Tetradontoidea; Tetraodontidae; Takifugu.
OX   NCBI_TaxID=31033;
RN   [1]
RP   SEQUENCE FROM N.A.
RX   MEDLINE=98252138; PubMed=9599080;
RA   Villard L., Tassone F., Crnogorac-Jurcevic T., Clancy K., Gardiner K.;
RT   "Analysis of pufferfish homologues of the AT-rich human APP gene.";
RL   Gene 210:17-24(1998).
```

```
CC   -!- FUNCTION: Functional neuronal receptor which couples to
CC       intracellular signaling pathway through the GTP-binding protein
CC       G(O) (By similarity).
CC   -!- SUBCELLULAR LOCATION: Type I membrane protein.
CC   -!- SIMILARITY: Belongs to the APP family.
CC   -!- SIMILARITY: Contains 1 BPTI/Kunitz inhibitor domain.
CC   ---------------------------------------------------------------------------
CC   This SWISS-PROT entry is copyright. It is produced through a collaboration
CC   between the Swiss Institute of Bioinformatics and the EMBL outstation -
CC   the European Bioinformatics Institute. There are no restrictions on its
CC   use by non-profit institutions as long as its content is in no way
CC   modified and this statement is not removed. Usage by and for commercial
CC   entities requires a license agreement (See http://www.isb-sib.ch/announce/
CC   or send an email to license@isb-sib.ch).
CC   ---------------------------------------------------------------------------
DR   EMBL; AF090120; AAD13392.1; -.
DR   HSSP; P05067; 1HZ3.
DR   InterPro; IPR008155; A4_APP.
DR   InterPro; IPR008154; A4_extra.
DR   InterPro; IPR001255; Beta-APP.
DR   InterPro; IPR002223; Kunitz_BPTI.
DR   Pfam; PF02177; A4_EXTRA; 1.
DR   Pfam; PF03494; Beta-APP; 1.
DR   Pfam; PF00014; Kunitz_BPTI; 1.
DR   PRINTS; PR00203; AMYLOIDA4.
DR   PRINTS; PR00759; BASICPTASE.
DR   ProDom; PD000222; Kunitz_BPTI; 1.
DR   SMART; SM00006; A4_EXTRA; 1.
DR   SMART; SM00131; KU; 1.
DR   PROSITE; PS00319; A4_EXTRA; FALSE_NEG.
DR   PROSITE; PS00320; A4_INTRA; 1.
DR   PROSITE; PS00280; BPTI_KUNITZ_1; 1.
DR   PROSITE; PS50279; BPTI_KUNITZ_2; 1.
KW   Glycoprotein; Amyloid; Neurone; Transmembrane; Signal;
KW   Serine protease inhibitor.
FT   SIGNAL        1     18       POTENTIAL.
FT   CHAIN        19    737       ALZHEIMER'S DISEASE AMYLOID A4
FT                                 PROTEIN HOMOLOG.
FT   CHAIN       639    681       BETA-AMYLOID PROTEIN (POTENTIAL).
FT   DOMAIN       19    668       EXTRACELLULAR (POTENTIAL).
FT   TRANSMEM    669    689       POTENTIAL.
FT   DOMAIN      690    737       CYTOPLASMIC (POTENTIAL).
FT   DOMAIN      286    344       BPTI/KUNITZ INHIBITOR.
FT   SITE        726    729       CLATHRIN-BINDING (BY SIMILARITY).
FT   ACT_SITE    300    301       REACTIVE BOND.
FT   DISULFID    290    340       BY SIMILARITY.
FT   DISULFID    299    323       BY SIMILARITY.
FT   DISULFID    315    336       BY SIMILARITY.
FT   CARBOHYD    522    522       N-LINKED (GLCNAC. . .) (POTENTIAL).
SQ   SEQUENCE   737 AA;  82856 MW;  6FAD01E2E3B2B7E2 CRC64;

  Query Match             78.0%;  Score 32;  DB 1;  Length 737;
  Best Local Similarity   85.7%;  Pred. No. 42;
  Matches    6;  Conservative    1;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 LVFFAED 7
              |||||:|
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Db 655 LVFFADD 661

Search completed: March 4, 2004, 15:36:27
Job time : 1.25532 secs